Library structure search

Checked JR 11-6-2006

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=> d his nofile

     (FILE 'HOME' ENTERED AT 15:00:43 ON 18 JUL 2006)

     FILE 'REGISTRY' ENTERED AT 15:00:48 ON 18 JUL 2006
L1             STRUCTURE UPLOADED
               D QUE L1
L2          25 SEA SSS SAM L1
L3         416 SEA SSS FUL L1

     FILE 'CAPLUS' ENTERED AT 15:01:59 ON 18 JUL 2006
L4          28 SEA ABB=ON  PLU=ON  L3
L5          12 SEA ABB=ON  PLU=ON  L4 NOT (PY>1999 OR AY>1999 OR PRY>1999)
               E KRATZ F/AU
L6          74 SEA ABB=ON  PLU=ON  ("KRATZ F"/AU OR "KRATZ FELIX"/AU)

=> file caplus
FILE 'CAPLUS' ENTERED AT 15:03:13 ON 18 JUL 2006
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FILE LAST UPDATED: 17 Jul 2006  (20060717/ED)

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http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

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L1             STR
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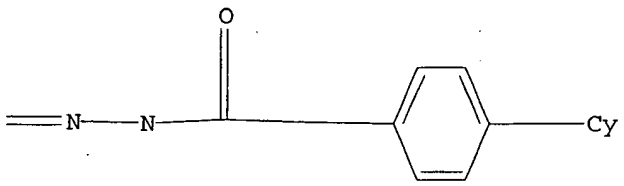


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Structure attributes must be viewed using STN Express query preparation.
L3         416 SEA FILE=REGISTRY SSS FUL L1
L4          28 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3
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Saloni Sharma

07/18/2006

=> d ibib abs hitstr l4 tot

L4 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1338574 CAPLUS
DOCUMENT NUMBER: 144:439737
TITLE: Structural optimization of a "smart" doxorubicin-polypeptide conjugate for thermally targeted delivery to solid tumors
AUTHOR(S): Furgeson, Darin Y.; Dreher, Matthew R.; Chilkoti, Ashutosh
CORPORATE SOURCE: Department of Biomedical Engineering, Duke University, Durham, NC, 27708-0281, USA
SOURCE: Journal of Controlled Release (2006), 110(2), 362-369
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

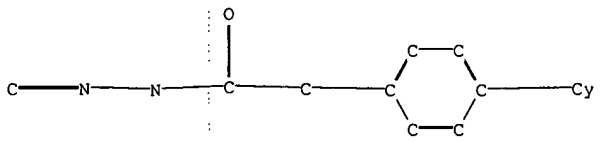
AB A thermoresponsive, genetically engineered, elastin-like polypeptide (ELP) containing a C-terminal cysteine residue was synthesized and purified by inverse transition cycling (ITC) and conjugated to doxorubicin (Dox) mols. through four different pH-sensitive, maleimide-activated, hydrazone linkers. The efficiency of Dox activation, conjugation ratios to ELP and biophys. characterization-hydrodynamic radius (Rh) and the temperature transition kinetics-of the ELP-Dox conjugates and pH-mediated release of Dox were quantified in this study. Conjugation ratios of the maleimide-activated Dox to the thiol group of a unique cysteine in the ELP were close to unity. The Rh of the conjugate increased as the linker length between the ELP backbone and Dox was increased. The linker structure and length had little effect on the Tt of the ELP-Dox conjugates, as all conjugates exhibited Tt's that were similar to the native ELP. However, the ELP-Dox conjugates with longer linkers exhibited slower transition kinetics compared to the ELP-Dox conjugates with shorter linkers. The highest release of the ELP-Dox conjugate by cleavage of the hydrazone bond at pH 4 was nearly 80% over 72 h and was exhibited by the conjugate with the shortest linker.

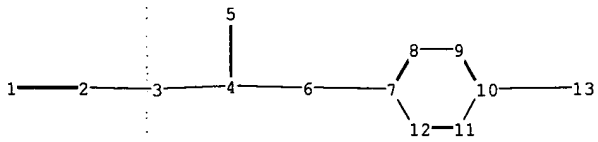
IT 202407-74-7D, conjugates with genetically engineered elastin-like polypeptide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structural optimization of a "smart" doxorubicin-polypeptide conjugate for thermally targeted delivery to solid tumors)

RN 202407-74-7 CAPLUS
CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

C:\Program Files\Stnexp\Queries\russel854broad.str





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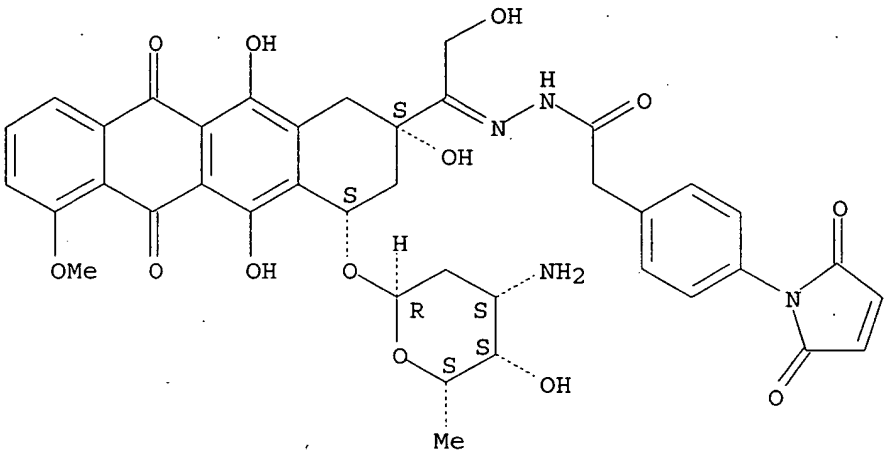
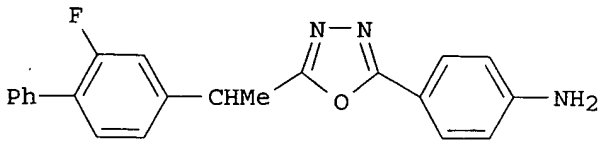
1 2 3 4 5 6 13
ring nodes :
7 8 9 10 11 12
chain bonds :
1-2 2-3 3-4 4-5 4-6 6-7 10-13
ring bonds :
7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 2-3 3-4 4-5 10-13
exact bonds :
4-6 6-7
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12

Match level :
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:Atom 8:Atom
9:Atom 10:Atom 11:Atom 12:Atom 13:Atom



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:265139 CAPLUS
DOCUMENT NUMBER: 143:405819
TITLE: Synthesis of some new 2-(2-fluoro-4-biphenylyl)propionic acid derivatives as potential anti-inflammatory agents
AUTHOR(S): Amir, M.; Kumar, S.
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Hamdard University, New Delhi, 110062, India
SOURCE: Pharmazie (2005), 60(3), 175-180
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:405819
GI



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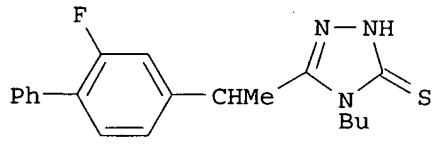

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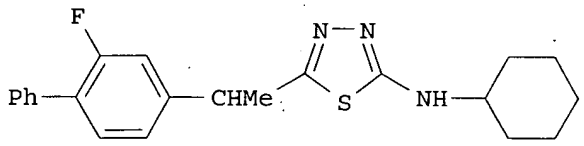
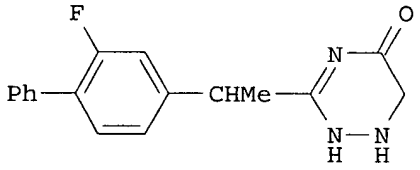


III



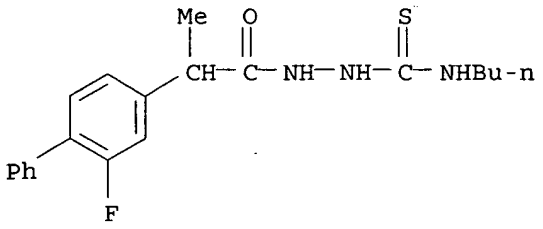
IV

AB The synthesis of a group of 1,3,4-oxadiazoles, e.g., I; 1,2,4-triazoles, e.g., II; 1,3,4-thiadiazoles, e.g., III; and a 1,2,4-triazine (IV) derived from 2-(2-fluoro-4-biphenylyl)propionic acid is described. The structures of the new compds. are supported by IR, 1H NMR and MS data. These compds. were tested in vivo for their anti-inflammatory activity. The compds. which showed activity comparable to the standard drug flurbiprofen were screened for their analgesic, ulcerogenic and lipid peroxidn. activities. Five out of 17 new compds. showed very good anti-inflammatory activity in the carrageenan induced rat paw edema test with negligible ulcerogenic action. The compds. which showed less ulcerogenic action also showed reduced malondialdehyde production, which is one of the byproducts of lipid peroxidn. The study showed that the compds. inhibit the induction of gastric mucosal lesions, and it can be suggested from our results that their protective effects may be related to an inhibition of lipid peroxidn. in the gastric mucosa.

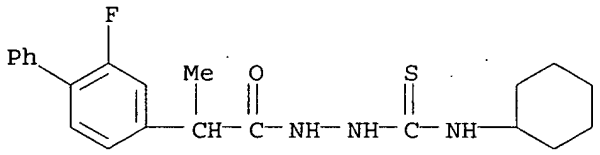
IT 867176-55-4P 867176-56-5P 867176-57-6P
867176-58-7P 867176-59-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
((fluorobiphenylyl)ethyl derivs. of heterocycles as potential anti-inflammatory agents)

RN 867176-55-4 CAPLUS

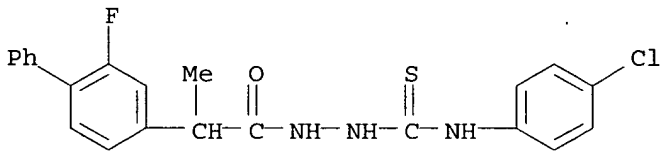
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[(butylamino)thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



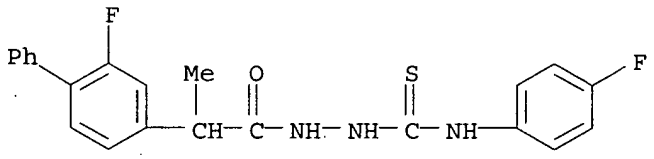
RN 867176-56-5 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[(cyclohexylamino)thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



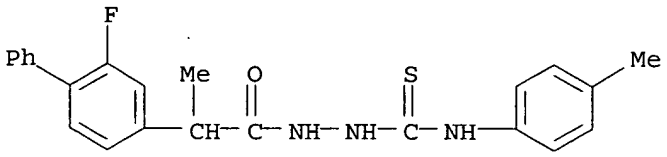
RN 867176-57-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[[(4-chlorophenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



RN 867176-58-7 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[[(4-fluorophenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



RN 867176-59-8 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[[(4-methylphenyl)amino]thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1022669 CAPLUS
DOCUMENT NUMBER: 141:420426
TITLE: Antineoplastic cytotoxic agent conjugates with transferrin, albumin and polyethylene glycol
INVENTOR(S): Kratz, Felix
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9810794	A2	19980319	WO 1997-DE2000	19970909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19636889	A1	19980312	DE 1996-19636889	19960911
CA 2265861	AA	19980319	CA 1997-2265861	19970909
AU 9745489	A1	19980402	AU 1997-45489	19970909
EP 934081	A2	19990811	EP 1997-943750	19970909
EP 934081	B1	20040609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500133	T2	20010109	JP 1998-513144	19970909
AT 268608	E	20040615	AT 1997-943750	19970909
US 6310039	B1	20011030	US 1999-254598	19990521
US 2002019343	A1	20020214	US 2001-931940	20010820
US 6709679	B2	20040323		

PRIORITY APPLN. INFO.:

DE 1996-19636889	A	19960911
WO 1997-DE2000	W	19970909
US 1999-254598	A1	19990521

OTHER SOURCE(S): MARPAT 141:420426

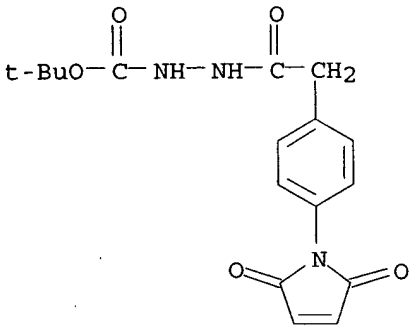
AB The invention discloses conjugates of (native or thiolated) transferrin or (native or thiolated) albumin, or of polyethylene glycol (approx. 5000-200,000 mol. weight) with at least one SH, OH or NH2 group, and cytostatic compds. (e.g. doxorubicin) derivatized through maleimide or N-hydroxysuccinimide ester-compds. Preparation of compds. and conjugates is included.

IT 188985-11-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antineoplastic cytotoxic agent conjugates with transferrin, albumin and polyethylene glycol)

RN 188985-11-7 CAPLUS

CN Hydrazinecarboxylic acid, 2-[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:565073 CAPLUS
DOCUMENT NUMBER: 141:117186
TITLE: Use of cathepsin k inhibitors for the treatment of glaucoma
INVENTOR(S): Shepard, Allan; Clark, Abbot F.; Jacobson, Nasreen
PATENT ASSIGNEE(S): Alcon, Inc., Switz.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058238	A1	20040715	WO 2003-US40511	20031219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003297363	A1	20040722	AU 2003-297363	20031219
US 2006020001	A1	20060126	US 2005-537052	20050602
PRIORITY APPLN. INFO.:			US 2002-436126P	P 20021223
			WO 2003-US40511	W 20031219

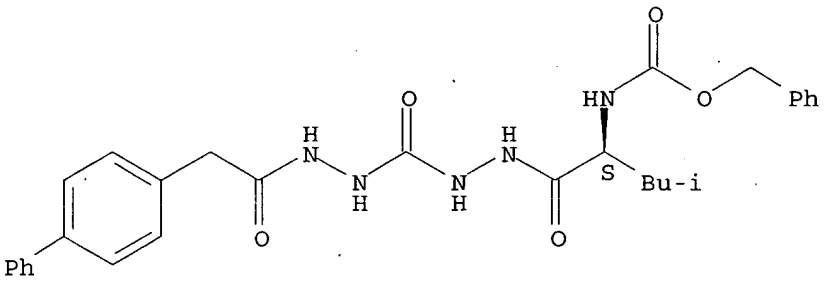
AB Compns. containing inhibitors of cathepsin K (CTSK) expression and/or activity are provided. Methods for the treatment of glaucoma using the compns. of the invention are further provided. The cathepsin K antagonist is selected from, but not limited to, the group consisting of monensin,

brefeldin A, tunicamycin and 1,3-bis(acylamino)-2-propanone derivs., cycloaltilisin 6, cycloaltilisin 7, AC-3-1, AC-3-3, AC-5-1, haloscleridamine, SB-331750, SB-357114, peptidomimetic aminomethyl ketones, α,α'-diacylamino ketones, alkoxymethyl ketones, cyanamides, pyridoxal propionate derivs. (including Clik-164 and Clik-166), SB-290190, α-alkoxy ketone derivs., cyanamide derivs., and Nα-acyl-α-amino acid-(arylaminoethyl)amides.

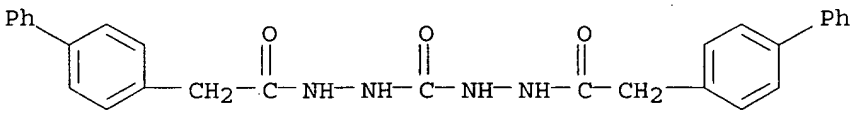
IT 190657-94-4 190657-96-6 190657-99-9
190658-00-5 190658-01-6 190658-05-0
190658-06-1 190658-07-2 190658-13-0
190658-18-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of cathepsin k inhibitors for treatment of glaucoma)

RN 190657-94-4 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

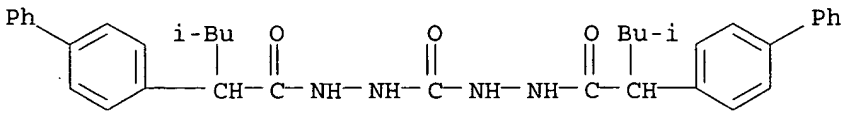
Absolute stereochemistry.



RN 190657-96-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2,2'-carbonyldihydrazide (9CI) (CA INDEX NAME)

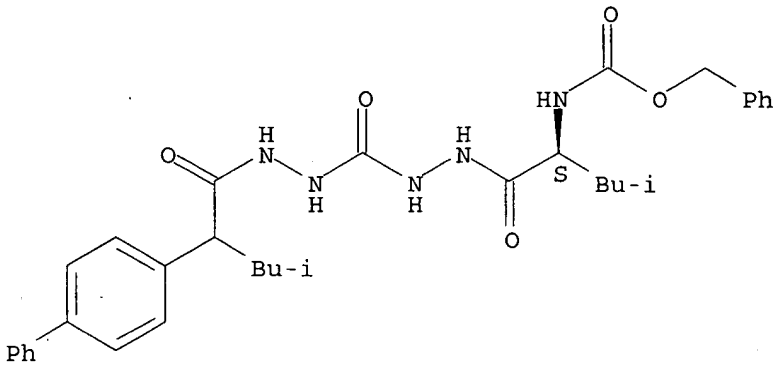


RN 190657-99-9 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2,2'-carbonyldihydrazide (9CI) (CA INDEX NAME)

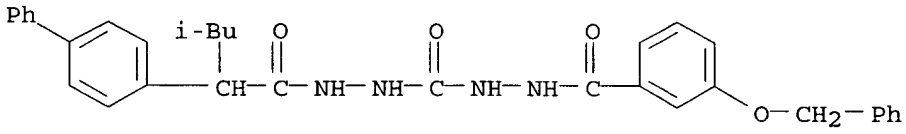


RN 190658-00-5 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

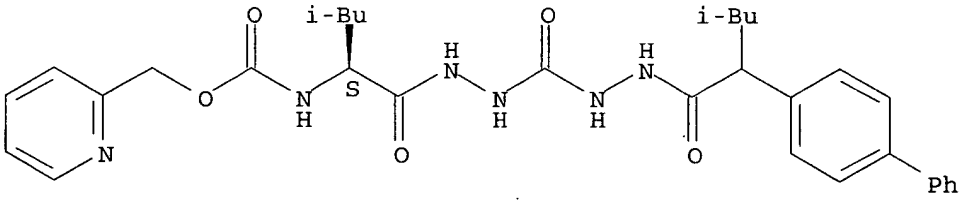


RN 190658-01-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[3-(phenylmethoxy)benzoyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)



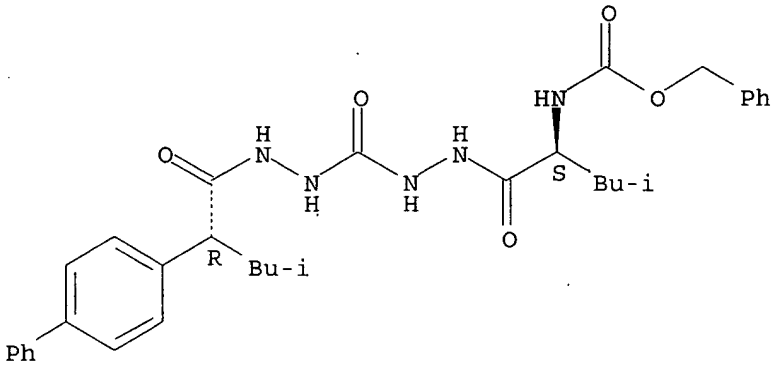
RN 190658-05-0 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(2-pyridinylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



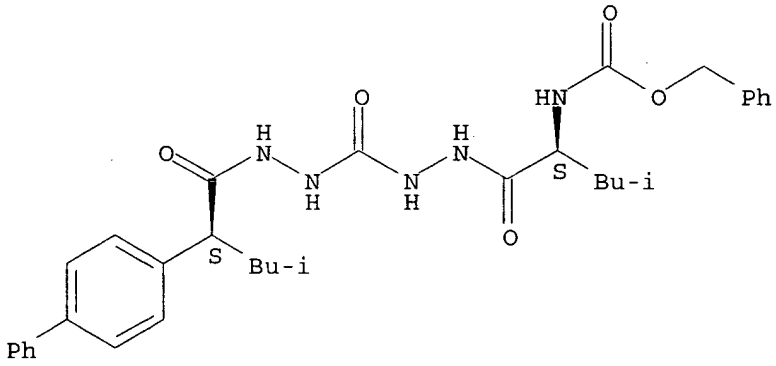
RN 190658-06-1 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



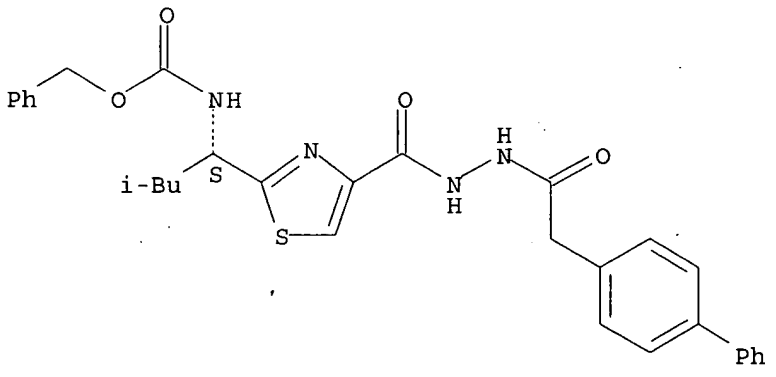
RN 190658-07-2 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



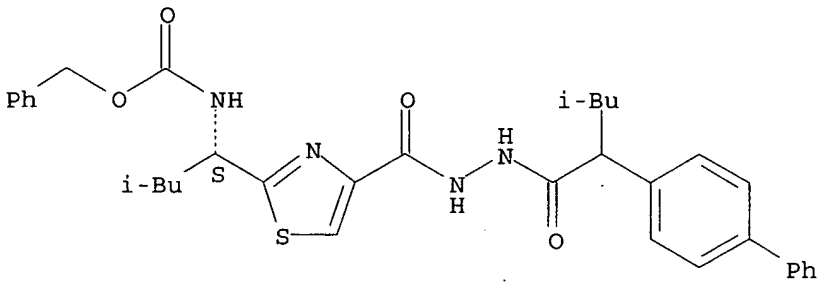
RN 190658-13-0 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(1S)-3-methyl-1-[[(phenylmethoxy)carbonyl]amino]butyl]-, 2-([1,1'-biphenyl]-4-ylacetyl)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190658-18-5 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(1S)-3-methyl-1-[[(phenylmethoxy)carbonyl]amino]butyl]-, 2-(2-[1,1'-biphenyl]-4-yl-4-methyl-1-oxopentyl)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:290470 CAPLUS
DOCUMENT NUMBER: 140:297550
TITLE: Methods and compositions using small organic molecules for modification of splicing of pre-mRNA, screening method, and therapeutic use
INVENTOR(S): Kole, Ryszard
PATENT ASSIGNEE(S): University of North Carolina At Chapel Hill, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004028464	A2	20040408	WO 2003-US30423	20030926
WO 2004028464	A3	20040708		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499880	AA	20040408	CA 2003-2499880	20030926
AU 2003278980	A1	20040419	AU 2003-278980	20030926
US 2004137472	A1	20040715	US 2003-672501	20030926
EP 1546733	A2	20050629	EP 2003-770490	20030926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006500933	T2	20060112	JP 2004-539981	20030926
PRIORITY APPLN. INFO.:			US 2002-414141P P	20020927
			WO 2003-US30423 W	20030926

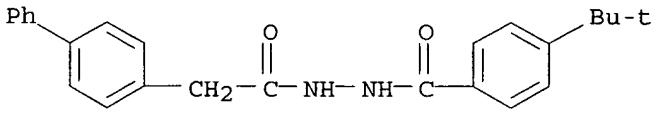
AB The invention provides a method for preventing a splicing event in a

pre-mRNA mol., comprising contacting the pre-mRNA and/or elements of the splicing machinery with a small mol. compound identified according to the methods of the invention to prevent the splicing event in the pre-mRNA mol. Also provided is a method for inducing a splicing event in a pre-mRNA mol., comprising contacting the pre-mRNA and/or elements of the splicing machinery with a small mol. compound identified according to the methods of the invention to induce the splicing event in the pre-mRNA mol. Furthermore, a method is provided for treating a patient having a disorder associated with an alternative or aberrant splicing event in a pre-mRNA mol., comprising administering to the patient a therapeutically effective amount of a compound identified according to the methods of the invention to prevent an alternative or aberrant splicing event in a pre-mRNA mol., thereby treating the patient.

IT 415694-94-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(small organic mols. for modification of splicing of pre-mRNA, screening method, and therapeutic use)

RN 415694-94-9 CAPLUS

CN [1,1'-Biphenyl]-4-acetic acid, 2-[4-(1,1-dimethylethyl)benzoyl]hydrazide (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:931171 CAPLUS

DOCUMENT NUMBER: 140:5052

TITLE: Preparation of 1,3,4-oxadiazoles and related compounds for use as melanin concentrating hormone antagonists in the treatment of obesity and diabetes

INVENTOR(S): Ammenn, Jochen; Gillig, James Ronald; Heinz, Lawrence Joseph; Hipskind, Philip Arthur; Kinnick, Michael Dean; Lai, Yen-shi; Morin, John Michael, Jr.; Nixon, James Arthur; Ott, Carsten; Savin, Kenneth Allen; Schotten, Theo; Slieker, Lawrence John; Snyder, Nancy June; Robertson, Michael Alan

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; et al.

SOURCE: PCT Int. Appl., 592 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097047	A1	20031127	WO 2003-US12123	20030506

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2484233	AA	20031127	CA 2003-2484233	20030506
AU 2003222648	A1	20031202	AU 2003-222648	20030506
EP 1505968	A1	20050216	EP 2003-719843	20030506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005529923	T2	20051006	JP 2004-505046	20030506
US 2005272718	A1	20051208	US 2005-512986	20050428
PRIORITY APPLN. INFO.:			US 2002-380351P	P 20020513
			WO 2003-US12123	W 20030506

OTHER SOURCE(S): MARPAT 140:5052

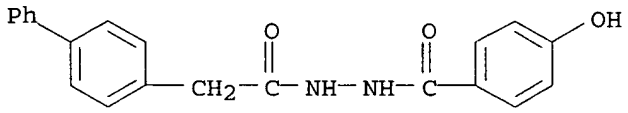
AB The present invention relates to 1,3,4-oxadiazoles and related compds. (Ar1-L1-Ar2-Ar3-L2-Q (I); variables defined below; e.g. N-(3-dimethylaminopropyl)-4-[5-(3-phenylpropoxymethyl)-[1,3,4]oxadiazol-2-yl]benzamide) as melanin concentrating hormone (MCH) antagonists or a pharmaceutically acceptable salt, solvate, enantiomer or prodrug thereof useful in the treatment, prevention or amelioration of symptoms associated with obesity and related diseases. Ki and Kb values for MCHR1 binding by 24 examples of (I) are tabulated. For Ar1-L1-Ar2-Ar3-L2-Q: Ar1 is a cyclic group (un)substituted with 1-5 C1-C8 alkyl, C2-C8 alkenyl, C2-C8 alkynyl, hydroxy, C1-C8 alkoxy, C1-C8 alkylaryl, Ph, -O-aryl, heteroaryl, cycloalkyl, C1-C8 alkylcycloalkyl, cyano, -(CH2)nNR6R6, C1-C8 haloalkyl, C1-C8 haloalkoxy, halo, (CH2)nCOR6, (CH2)nNR5SO2R6, -(CH2)nC(O)NR6R6, heterocyclic, and C1-C8 alkylheterocyclic. L1 is a bond or a divalent linker having a main chain = 1-10 atoms; or X2-(CR3R4)m-X3 where X2 is attached to Ar1 and X3 is attached to Ar2 wherein R3 and R4 = a bond, H, C1-C8 alkyl, C2-C8 alkylene, C2-C8 alkynyl, Ph, aryl, C1-C8 alkylaryl; X2 = O, -CH, -CONH(CR3R4)m, -NHCO(CR3R4)m, - (CR3R4)m, -CHR6, -NR5, S, SO, SO2, -O(CR3R4)m, or -S(CR3R4)m; X3 = O, -C, -CH, -CHR6, -(CR3R4)m, -CONH(CR3R4)m, -NHCO(CR3R4)m, -NR5, -NR5(CR3R4)m, S, SO(CR3R4)m, SO2(CR3R4)m, S(CR3R4)m, SO, or SO2; -O(CR3R4)m, or -S(CR3R4)m; Ar2 is a 5-member monocyclic heterocyclic aromatic group or positional isomer thereof, having 1, 2, or 3 heteroatoms = N, O and S; and (un)substituted with one to three substituents. Ar3 is a 6-member monocyclic, aromatic, carbocyclic or heterocyclic ring having 0-3 heteroatoms = N, O and S and which is (un)substituted with 1-3 substituents; L2 is a divalent linker having a chain length = 1-10 atoms in the main chain or is represented by the formula: X4-(CR3R4)m-X5; wherein X4 is attached to Ar3 and = C, -CH, CHR6, -CO, O, -NR5, -NC(O)-, -NC(S), -C(O)NR5-, -NR6C(O)NR6, -NR6'C(S)-NR6, -SO2NR7, - NRSO2R7, and -NR6'C(NR5)NR6; X5 = -CH2, -CH, -O(CR3R4)m, NR3(CR3R4)m, SO, SO2, S, and SCH2; wherein the group X4-(CR3R4)m-X5 imparts stability and may be a (un)saturated chain or divalent linker. Q is a basic group or a group represented by -NR1R2; wherein R1 and R2 = H, C1-C8 alkyl, C2-C8 alkenyl, C3-C8 cycloalkyl, C1-C8 alkylaryl, -C(O)C1-C8 alkyl, -C(O)OC1-C8 alkyl, C1-C8 alkylcycloalkyl, (CH2)nC(O)OR5, (CH2)nC(O)R5, (CH2)nC(O)NR6R6, and (CH2)nNSO2R5; wherein R1 and R2 may combine together, and with the N atom to which they are attached or with 0-3 atoms adjacent to the N atom to form a N containing heterocycle which may have 1, or 2 substituents; wherein R1 and R2 may combine with the N atom to which they are attached to form an imine. R5 is H, CN, C1-C8 alkyl, C2-C8 alkenyl, C5-C8 alkylaryl, (CH2)nNSO2C1-C8 alkyl, (CH2)nNSO2phenyl, (CH2)nNSO2aryl, -C(O)C1-C8 alkyl, or -C(O)OC1-C8 alkyl; and R6 and R6' are each independently H, C1-C8 alkyl, Ph, aryl, C1-C8alkylaryl, or C3-C8cycloalkyl; R7 is H, C1-C8 alkyl, Ph, aryl, C1-C8alkylaryl, or C3-C8cycloalkyl, and wherein m = 1-8; and n = 0-8; addnl. details including provisos are given in the claims. Although the methods of

preparation are not claimed, >300 example prepns. are included.

IT 627901-33-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1,3,4-oxadiazoles and related compds. for use as melanin concentrating hormone antagonists in treatment of obesity and diabetes)

RN 627901-33-1 CAPLUS

CN [1,1'-Biphenyl]-4-acetic acid, 2-(4-hydroxybenzoyl)hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:817501 CAPLUS

DOCUMENT NUMBER: 140:326874

TITLE: Novel daunorubicin-carrier peptide conjugates derived from human calcitonin segments

AUTHOR(S): Krauss, Ulrike; Kratz, Felix; Beck-Sickinger, Annette G.

CORPORATE SOURCE: Institute of Biochemistry, University of Leipzig, Leipzig, 04103, Germany

SOURCE: Journal of Molecular Recognition (2003), 16(5), 280-287
CODEN: JMORE4; ISSN: 0952-3499

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

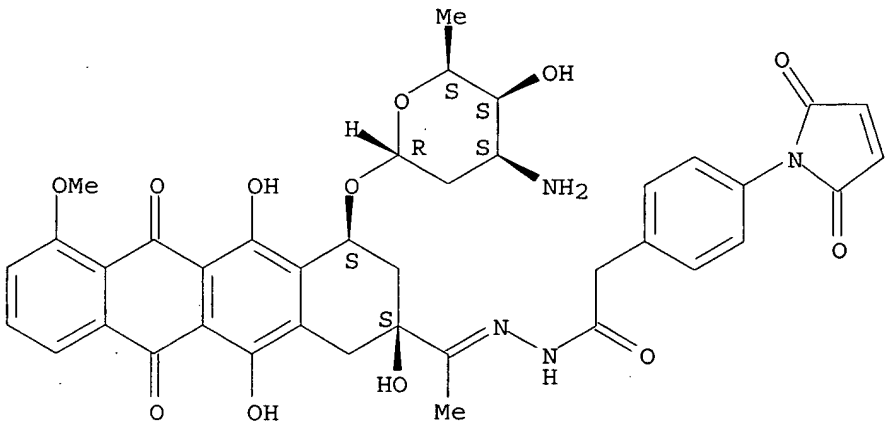
AB Severe and often therapy-limiting side effects are a major obstacle in cancer chemotherapy. New delivery concepts reducing systemic side effects are needed in order to optimize anticancer therapies. Several approaches have been followed, most of them concentrating on macromol. carriers like liposomes, monoclonal antibodies, serum proteins or polyethylene glycol. We present here a novel type of anthracycline conjugate, using a small carrier peptide derived from the peptide hormone human calcitonin (hCT). The carrier peptide hCT(9-32) has so far been shown to be capable of transporting fluorophores or proteins across cellular membranes. Two different carrier peptide-daunorubicin conjugates were prepared, one with an acid-stable amide bond, the second with an acid-labile hydrazone bond. In vitro studies with daunorubicin linked to the carrier peptide via an acid-labile hydrazone bond demonstrated comparable cytotoxicity to daunorubicin in various daunorubicin sensitive cell lines (neuroblastoma cell lines SK-N-MC and SMS-KAN; HEK 293 T cells). In addition, fluorescence microscopy provided further insight into the mechanism of uptake of the carrier peptide hCT(9-32), indicating that endosomal compartments with reduced pH are involved in the intracellular release of daunorubicin.

IT 342607-67-4DP, human calcitonin peptide derivs.
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel daunorubicin-carrier peptide conjugates derived from human calcitonin segments)

RN 342607-67-4 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]ethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:11099 CAPLUS
DOCUMENT NUMBER: 136:69597
TITLE: Synthesis of hydrazide and α-alkoxyamide angiogenesis inhibitors
INVENTOR(S): Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.; Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 78 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002002152	A1	20020103	US 2001-833917	20010412
US 2004167126	A1	20040826	US 2004-782502	20040219
US 6887863	B2	20050503		
PRIORITY APPLN. INFO.:			US 2000-197262P P	20000414
			US 2001-833917 A1	20010412

OTHER SOURCE(S): MARPAT 136:69597
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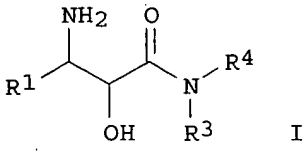

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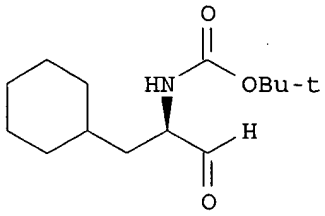

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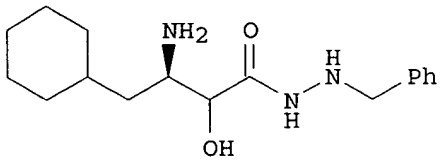


III

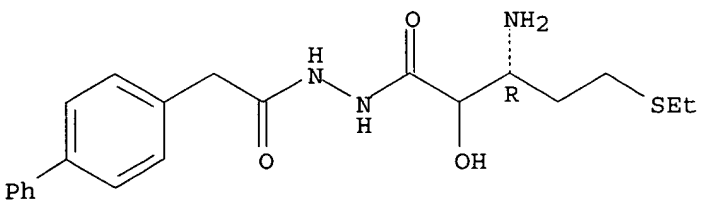
AB Title compds. I [R1 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R5S-alkylene; R3 = H, alkyl, arylalkyl; R4 = NR6R7, OR8; R5 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R6-7 = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R6-7 together are arylalkylidene; or R6-7 together with the nitrogen atom to which they are attached, form a heterocycle; R8 = H, alkanoylalkyl, alkenyl, alkoxycarbonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R9-10 = H, alkyl, aryl] were prepared Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0°C, room temperature 1 h) and oxidized to II (DMSO, Py•SO3, Et3N, room temperature 30 min). II was converted to the bisulfite addition product (H2O, NaHSO3, 5°C, 24 h) and reacted with KCN to give the α-hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBt). Selected compds. I had IC50 < 0.1 μM for MetAP2. I are useful for inhibiting angiogenesis.

IT 369358-55-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of hydrazide and α-alkoxyamide angiogenesis inhibitors)

RN 369358-55-4 CAPLUS

CN D-glycero-Pentonic acid, 3-amino-3,4-dideoxy-5-S-ethyl-5-thio-, 2-([1,1'-biphenyl]-4-ylacetyl)hydrazide, (2ξ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:780840 CAPLUS
DOCUMENT NUMBER: 135:331197
TITLE: Synthesis of hydrazide and α-alkoxyamide angiogenesis inhibitors
INVENTOR(S): Craig, Richard A.; Kawai, Megumi; Lynch, Linda M.; Patel, Jyoti R.; Sheppard, George S.; Wang, Jieyi; Yang, Fan; Ba-Maung, Nwe Y.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079157	A1	20011025	WO 2001-US12274	20010413
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2406442	AA	20011025	CA 2001-2406442	20010413
EP 1272456	A1	20030108	EP 2001-925029	20010413
EP 1272456	B1	20041027		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001007204	A	20040225	BR 2001-7204	20010413
JP 2004509063	T2	20040325	JP 2001-576759	20010413
AT 280753	E	20041115	AT 2001-925029	20010413
PT 1272456	T	20050228	PT 2001-925029	20010413
ES 2231475	T3	20050516	ES 2001-1925029	20010413
HK 1053825	A1	20050819	HK 2003-104469	20030620
PRIORITY APPLN. INFO.:			US 2000-549995 A	20000414
			US 2001-813008 A	20010321
			WO 2001-US12274 W	20010413

OTHER SOURCE(S): MARPAT 135:331197
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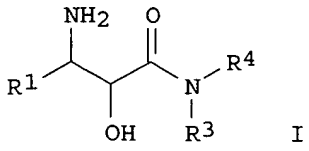

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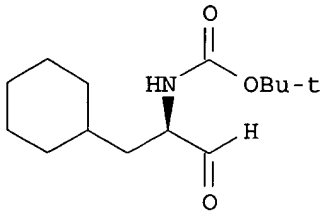

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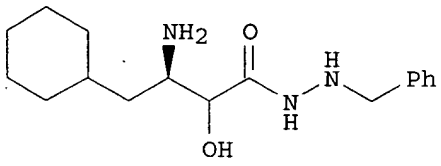


III

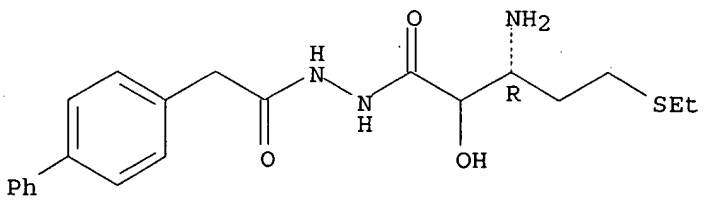
AB Title compds. I [R1 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocycle)alkyl, R5S-alkylene; R3 = H, alkyl, arylalkyl; R4 = NR6R7, OR8; R5 = alkyl, aryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl; R6-7 = H, alkanoyl, alkenyl, alkenyloxyalkyl, alkoxyalkyl, alkoxycarbonylalkyl, alkyl, alkylthioalkyl, aryl, arylalkanoyl, etc.; or R6-7 together are arylalkylidene; or R6-7 together with the nitrogen atom to which they are attached, form a heterocycle; R8 = H, alkanoylalkyl, alkenyl, alkoxycarbonylalkyl, alkyl, amidoalkyl, aryl, arylalkyl, etc.; R9-10 = H, alkyl, aryl] were prepared Over 450 synthetic examples were reported. For instance, (2R)-2-(Boc)amino-3-cyclohexylpropanoic acid was reduced to the corresponding alc. (PhMe, Red-Al, 0°C, room temperature 1 h) and oxidized to II (DMSO, Py•SO3, Et3N, room temperature 30 min). II was converted to the bisulfite addition product (H2O, NaHSO3, 5°C, 24 h) and reacted with KCN to give the α-hydroxy nitrile intermediate which was hydrolyzed to the carboxylic acid (12 N HCl, reflux, 21 h) and converted to III by condensation with benzylhydrazine (DCM/DMA, DIC, NMM, HOBt). Selected compds. I had IC50 < 0.1 μM for MetAP2. I are useful for inhibiting angiogenesis.

IT 369358-55-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of hydrazide and α-alkoxyamide angiogenesis inhibitors)

RN 369358-55-4 CAPLUS

CN D-glycero-Pentonic acid, 3-amino-3,4-dideoxy-5-S-ethyl-5-thio-, 2-([1,1'-biphenyl]-4-ylacetyl)hydrazide, (2ξ)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN

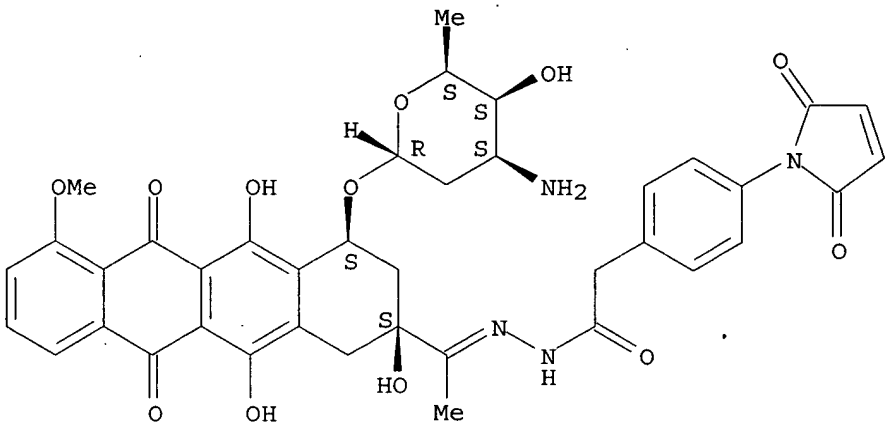
ACCESSION NUMBER: 2001:238414 CAPLUS
DOCUMENT NUMBER: 135:24537
TITLE: Novel peptide conjugates for tumor-specific chemotherapy
AUTHOR(S): Langer, Michael; Kratz, Felix; Rothen-Rutishauser, Barbara; Wunderli-Allenspach, Heidi; Beck-Sickinger, Annette G.
CORPORATE SOURCE: Institute of Biochemistry, University of Leipzig, Leipzig, D-04103, Germany
SOURCE: Journal of Medicinal Chemistry (2001), 44(9), 1341-1348
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB One of the major problems in cancer chemotherapy are the severe side effects that limit the dose of the anticancer drugs because of their unselectivity for tumor vs. normal cells. In the present work, we show that coupling of anthracyclines to peptides is a promising approach to obtain selectivity. The peptide-drug conjugate was designed to bind to specific receptors expressed on the tumor cells with subsequent internalization of the ligand-receptor complex. Neuropeptide Y (NPY), a 36-amino acid peptide of the pancreatic polypeptide family, was chosen as model peptide because NPY receptors are overexpressed in a number of neuroblastoma tumors and the thereof derived cell lines. Daunorubicin and doxorubicin, two widely used antineoplastic agents in tumor therapy, were covalently linked to NPY via two spacers that differ in stability: an acid-sensitive hydrazone bond at the 13-keto position of daunorubicin and a stable amide bond at the 3'-amino position of daunorubicin and doxorubicin. Receptor binding of these three conjugates ([C15]-NPY-Dauno-HYD, [C15]-NPY-Dauno-MBS, and [C15]-NPY-Doxo-MBS) was determined at the human neuroblastoma cell line SK-N-MC, which selectively expresses the NPY Y1 receptor subtype, and cytotoxic activity was evaluated using a XTT-based colorimetric cellular cytotoxicity assay. The different conjugates were able to bind to the receptor with affinities ranging from 25 to 51 nM, but only the compound containing the acid-sensitive bond ([C15]-NPY-Dauno-HYD) showed cytotoxic activity comparable to the free daunorubicin. This cytotoxicity is Y1 receptor-mediated as shown in blocking studies with BIBP 3226, because tumor cells that do not express NPY receptors were sensitive to free daunorubicin, but not to the peptide-drug conjugate. The intracellular distribution was investigated by confocal laser scanning microscopy. We found evidence that the active conjugate [C15]-NPY-Dauno-HYD releases daunorubicin, which is localized close to the nucleus, whereas the inactive conjugate [C15]-NPY-Dauno-MBS is distributed distantly from the nucleus and does not seem to release the drug within the cell.

IT 342607-67-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(peptide conjugates for tumor-specific chemotherapy)

RN 342607-67-4 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]ethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:880603 CAPLUS
DOCUMENT NUMBER: 134:46760
TITLE: Drug-carrier conjugates for drug delivery
INVENTOR(S): Kratz, Felix
PATENT ASSIGNEE(S): KTB Tumorforschungsgesellschaft m.b.H., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19926475	A1	20001214	DE 1999-19926475	19990610
WO 2000076550	A2	20001221	WO 2000-EP5254	20000607
WO 2000076550	A3	20010517		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1198254	A2	20020424	EP 2000-943777	20000607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003501485	T2	20030114	JP 2001-502881	20000607
PRIORITY APPLN. INFO.:			DE 1999-19926475 A	19990610
			WO 2000-EP5254 W	20000607

AB Conjugates of drugs with carrier mols. are disclosed in which the carrier is a polypeptide mol. bearing one or more cysteine residue and the drug is

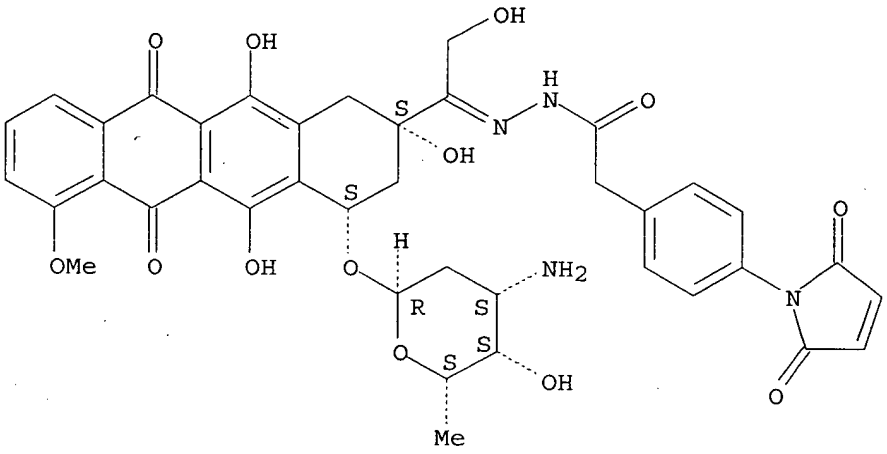
joined to a spacer mol. that has a thiol-binding group, so that for each mole of cysteine >0.7 mol of drug is bound to the carrier by means of the thiol-binding group. An example is presented of doxorubicin linked to a spacer joined to a maleimide group which, in turn, can form conjugates with cysteine residues of human serum albumin.

IT 312732-37-9P
RL: PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(drug-carrier conjugates for drug delivery)

RN 312732-37-9 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

L4 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:880585 CAPLUS
DOCUMENT NUMBER: 134:46759
TITLE: Procedure for the production of an injectable drug preparation
INVENTOR(S): Kratz, Felix
PATENT ASSIGNEE(S): KTB Tumorforschungsgesellschaft m.b.H., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 19926154	A1	20001214	DE 1999-19926154	19990609
CA 2374964	AA	20001221	CA 2000-2374964	20000607
WO 2000076551	A2	20001221	WO 2000-EP5272	20000607
WO 2000076551	A3	20010816		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1183050	A2	20020306	EP 2000-945721	20000607

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003501486	T2	20030114	JP 2001-502882	20000607
AU 779697	B2	20050210	AU 2000-59709	20000607
PRIORITY APPLN. INFO.:			DE 1999-19926154	A 19990609
			WO 2000-EP5272	W 20000607

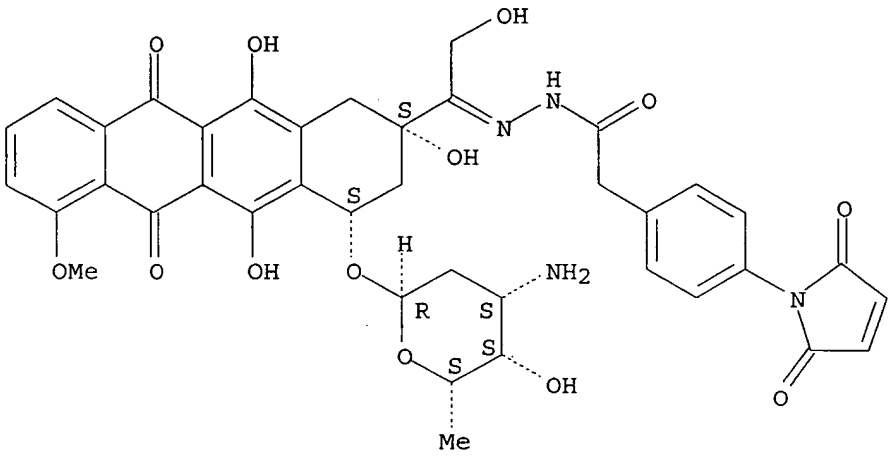
AB An injectable drug form is disclosed in which the pharmacol. active agent is connected by means of a spacer mol. to a protein-binding moiety which allows the drug to bind to serum proteins such as albumins. The linkage between the drug and the spacer is pH-dependent or enzymically cleavable in the body, so that the active agent can be released at the target site. An example is given in which doxorubicin is linked to a phenylacetylhydrazone spacer which bears a maleimide group as the protein-binding moiety.

IT 312732-37-9P
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(procedure for the production of an injectable drug preparation)

RN 312732-37-9 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:158262 CAPLUS
DOCUMENT NUMBER: 132:339173
TITLE: A Novel Macromolecular Prodrug Concept Exploiting Endogenous Serum Albumin as a Drug Carrier for Cancer Chemotherapy
AUTHOR(S): Kratz, Felix; Mueller-Driver, Ralph; Hofmann, Inga; Drevs, Joachim; Unger, Clemens
CORPORATE SOURCE: Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Journal of Medicinal Chemistry (2000), 43(7), 1253-1256
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A maleimide phenylacetylhydrazone derivative of doxorubicin (I) bound preferentially to endogenous serum albumin after incubation with human blood plasma or direct i.v. injection into mice. Preincubation studies with a maleimide compound and coupling reactions with native serum albumin indicate that I binds to cytosine-34 of albumin which is an attractive binding site in blood plasma due to the fact that other major plasma proteins do not contain free HS groups. In addition, I showed a superior antitumor effect in an animal tumor model, i.e., murine renal cell carcinoma (RENCA), when compared to free doxorubicin at equitoxic dose. This increase in therapeutic efficacy can be best explained by an enhanced permeability of tumor blood vessels for circulating proteins and a subsequent retention due to lacking lymphatic recovery system in tumor tissue. Studies in the RENCA model have shown that renal cell carcinomas are highly vascularized indicating that circulating macromols. such as serum albumin and resp. conjugates might be trapped by the vascular network of these tumors. Although a more detailed anal. of the in situ coupling of thiol-binding drug derivs. to endogenous albumin is warranted, it is believed that the outlined macromol. prodrug strategy is an attractive approach of altering the pharmacokinetic profile of clin.

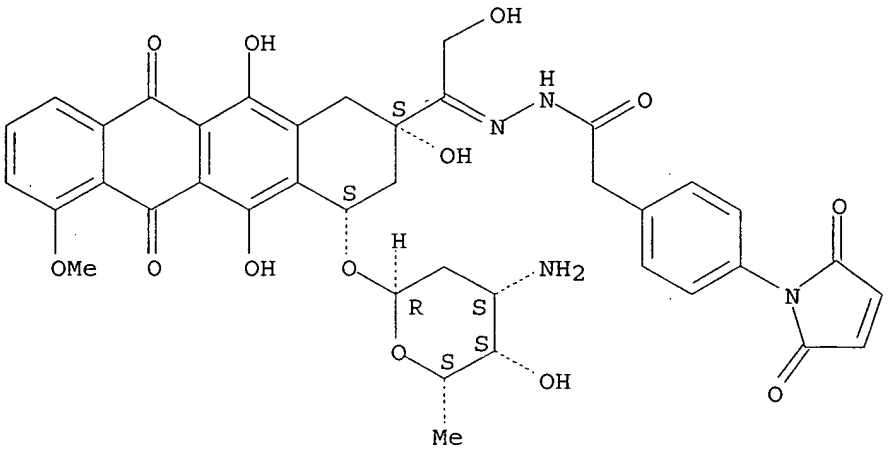
established anticancer drugs and increasing their therapeutic index.

IT 202407-74-7
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(macromol. prodrug concept exploiting endogenous serum albumin as drug carrier for cancer chemotherapy)

RN 202407-74-7 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

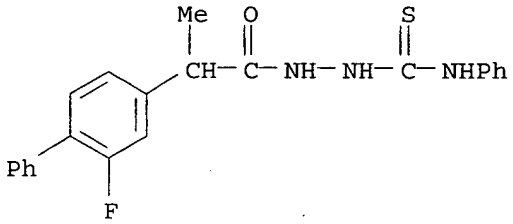
L4 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:442650 CAPLUS
DOCUMENT NUMBER: 131:242771
TITLE: Synthesis and biological evaluation of novel heterocyclic derivatives of flurbiprofen
AUTHOR(S): El-Sadek, Mohamed; Abdel-Aziz, Lubna M.; Kull, Mansour Abou; Metwally, Kamel A.
CORPORATE SOURCE: Dept. of Medicinal Chemistry, Faculty of Pharmacy, University of Zagazig, Zagazig, Egypt
SOURCE: Zagazig Journal of Pharmaceutical Sciences (1998), 7(1), 94-100
CODEN: ZJPSEV; ISSN: 1110-5089
PUBLISHER: University of Zagazig, Faculty of Pharmacy
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of some novel noncarboxylic heterocyclic derivs. of flurbiprofen such as pyrazole, pyrrole, oxadiazole, oxadiazines, and triazoles, is described. Three representative compds. were tested for analgesic, antipyretic, and antiinflammatory activities.

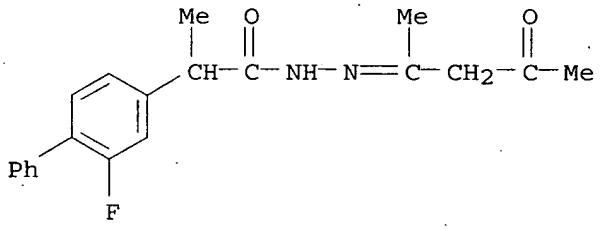
IT 244161-21-5P 244161-30-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and analgesic, antipyretic, and antiinflammatory activities of heterocyclic derivs. of flurbiprofen)

RN 244161-21-5 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, 2-[(phenylamino)thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



RN 244161-30-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, (1-methyl-3-oxobutylidene)hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

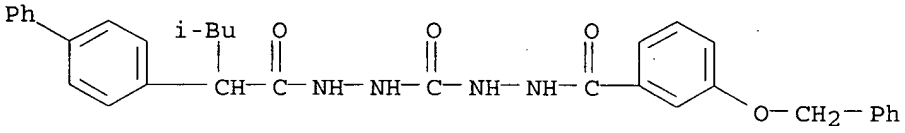
L4 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:269556 CAPLUS
DOCUMENT NUMBER: 131:53578
TITLE: Structure-based design of non-peptide, carbohydrazide-based cathepsin K inhibitors
AUTHOR(S): Thompson, Scott K.; Halbert, Stacie M.; DesJarlais, Renee L.; Tomaszek, Thaddeus A.; Levy, Mark A.; Tew, David G.; Ijames, Carl F.; Veber, Daniel F.
CORPORATE SOURCE: Department of Medicinal Chemistry, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(4), 599-605
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using binding models which were based on the X-ray crystal structure of an amino acid-based active site-spanning inhibitor complexed with cathepsin K, Cbz-leucine mimics have been developed, leading ultimately to the design of a potent cathepsin K inhibitor free of amino acid components. These mimics, which consist of α-substituted biphenylacetyl groups in place of Cbz-leucine moieties, effectively mimic all aspects of the Cbz-leucine moieties which are important for inhibitor binding. The predicted directions of binding for the inhibitors were confirmed by mass spectral anal. of their complexes with cathepsin K, which gave results

consistent with acylation of the enzyme and loss of the acylhydrazine portion of the inhibitor which binds on the S' side of the active site. The binding models were found to be very predictive of relative inhibitor potency as well as direction of inhibitor binding. These results strengthen the validity of a strategy involving iterative cycles of structure-based design and inhibitor synthesis and evaluation for the discovery of non-peptide inhibitors.

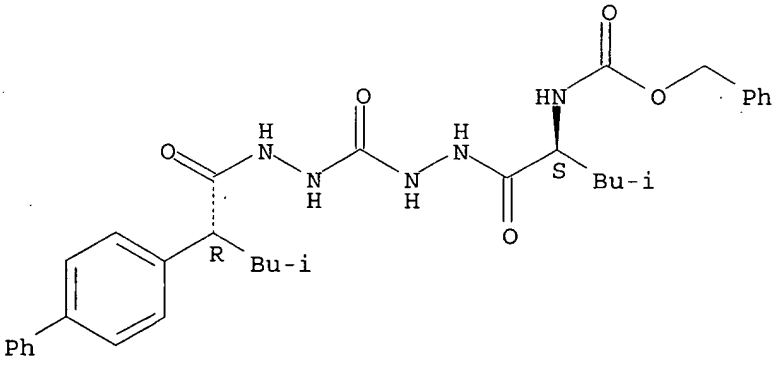
IT 190658-01-6P 190658-06-1P 190658-07-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-based design of non-peptide, carbohydrazide-based cathepsin K inhibitors)

RN 190658-01-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[3-(phenylmethoxy)benzoyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)



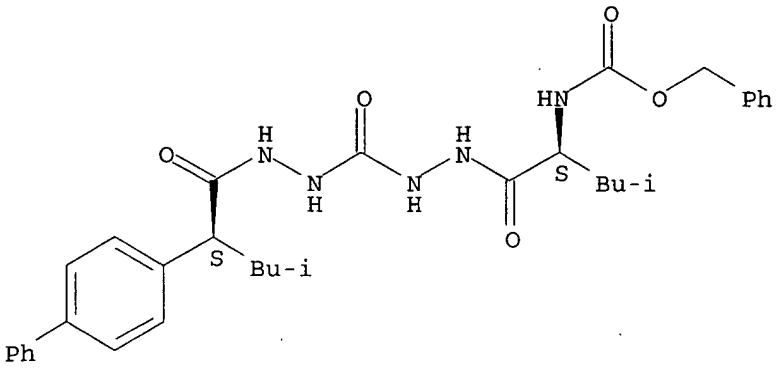
RN 190658-06-1 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 190658-07-2 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



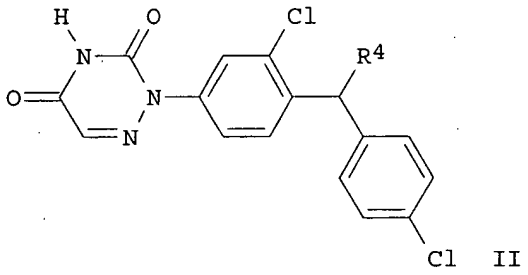
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:64782 CAPLUS
DOCUMENT NUMBER: 130:139366
TITLE: Preparation of 6-azauracil derivatives as IL-5 biosynthesis inhibitors
INVENTOR(S): Lacrampe, Jean Fernand Armand; Freyne, Eddy Jean Edgard; Venet, Marc Gaston; Boeckx, Gustaaf Maria
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902505	A1	19990121	WO 1998-EP4191	19980707
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2294145	AA	19990121	CA 1998-2294145	19980707
AU 9889738	A1	19990208	AU 1998-89738	19980707
AU 742145	B2	20011220		
EP 1000040	A1	20000517	EP 1998-941299	19980707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200000153	T2	20000721	TR 2000-200000153	19980707
EE 200000016	A	20001016	EE 2000-16	19980707
NZ 502180	A	20001124	NZ 1998-502180	19980707
TW 496865	B	20020801	TW 1998-87111014	19980708
ZA 9806089	A	20000110	ZA 1998-6089	19980709
BR 9811678	A	20000919	BR 1998-11678	19980710
HR 2000000003	A1	20001231	HR 2000-3	20000105
NO 2000000063	A	20000310	NO 2000-63	20000106
US 2002072603	A1	20020613	US 2001-891888	20010626

US 6867207	B2	20050315			
US 2005090495	A1	20050428	US 2003-671205		20030925
US 2004167333	A1	20040826	US 2004-782200		20040219
PRIORITY APPLN. INFO.:			EP 1997-202118	A	19970710
			WO 1998-EP4191	W	19980707
			US 2000-462320	B1	20000105
			US 2001-891888	A3	20010626

OTHER SOURCE(S): MARPAT 130:139366
GI



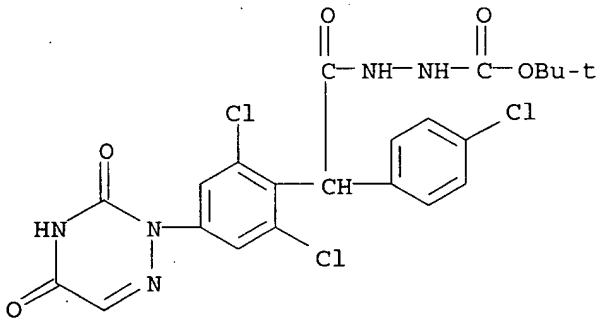
II

AB RZCR1(XR2)R3 [I; R= 3,5-dioxo-1,2,4-triazin-2(3H)-yl; R1 = H, halo, alkyl, alkoxy, etc.; R2 = CONH2, (un)substituted alkyl, (hetero)aryl, etc.; R3 = (un)substituted Ph; X = bond, O, s, (alkyl)imino; Z = (un)substituted phenylene] were prepared Thus, title compound II (R4 = Cl) was etherified by Me2CHCH2OH to give II (R4 = OCH2CHMe2). Data for biol. activity of I were given.

IT 219981-43-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 6-azauracil derivs. as IL-5 biosynthesis inhibitors)

RN 219981-43-8 CAPLUS

CN Hydrazinecarboxylic acid, 2-[(4-chlorophenyl)[2,6-dichloro-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl)phenyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

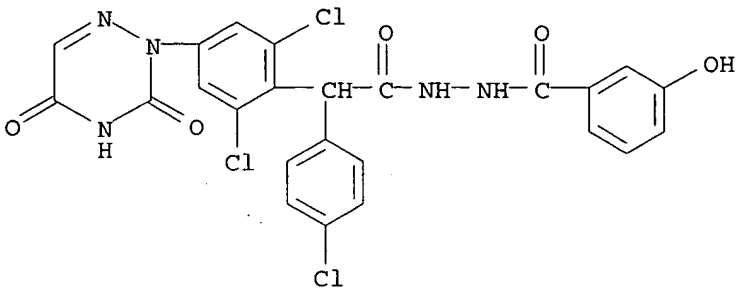


IT 219981-32-5P 219981-40-5P 219981-41-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 6-azauracil derivs. as IL-5 biosynthesis inhibitors)

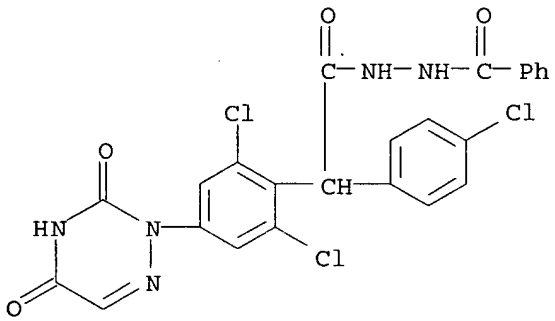
RN 219981-32-5 CAPLUS

CN Benzeneacetic acid, 2,6-dichloro-α-(4-chlorophenyl)-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl)-, 2-(3-hydroxybenzoyl)hydrazide (9CI)

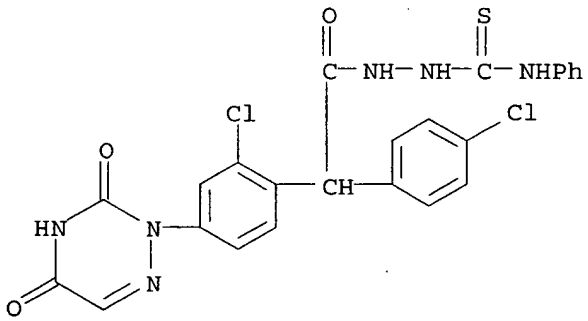
(CA INDEX NAME)



RN 219981-40-5 CAPLUS
CN Benzeneacetic acid, 2,6-dichloro-α-(4-chlorophenyl)-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl)-, 2-benzoylhydrazide (9CI) (CA INDEX NAME)



RN 219981-41-6 CAPLUS
CN Benzeneacetic acid, 2-chloro-α-(4-chlorophenyl)-4-(4,5-dihydro-3,5-dioxo-1,2,4-triazin-2(3H)-yl)-, 2-[(phenylamino)thioxomethyl]hydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:186637 CAPLUS
DOCUMENT NUMBER: 128:213389

TITLE: Antineoplastic transferrin and albumin conjugates of cytostatic compounds selected from anthracyclines, alkylating agents, antimetabolites, and cisplatin analogs

INVENTOR(S): Kratz, Felix

PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19636889	A1	19980312	DE 1996-19636889	19960911
CA 2265861	AA	19980319	CA 1997-2265861	19970909
WO 9810794	A2	19980319	WO 1997-DE2000	19970909
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9745489	A1	19980402	AU 1997-45489	19970909
EP 934081	A2	19990811	EP 1997-943750	19970909
EP 934081	B1	20040609		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500133	T2	20010109	JP 1998-513144	19970909
AT 268608	E	20040615	AT 1997-943750	19970909
EP 1447099	A2	20040818	EP 2004-12346	19970909
EP 1447099	A3	20050209		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6310039	B1	20011030	US 1999-254598	19990521
US 2002019343	A1	20020214	US 2001-931940	20010820
US 6709679	B2	20040323		

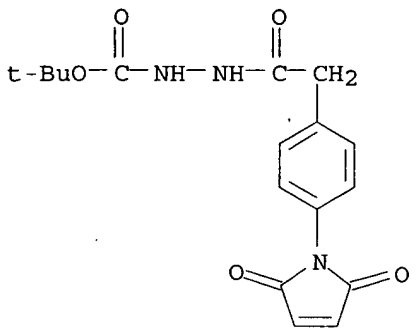
PRIORITY APPLN. INFO.:

DE 1996-19636889	A	19960911
EP 1997-943750	A3	19970909
WO 1997-DE2000	W	19970909
US 1999-254598	A1	19990521

OTHER SOURCE(S): MARPAT 128:213389

AB Conjugates of thiolated transferrin and/or albumin with maleimide-derivatized anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin), alkylating agents (chlorambucil, melphalan), antimetabolites (5-fluorouracil, 5'-deoxy-5-fluorouridine), or cisplatin analogs, where the linkage is through an amide, ester, imine, hydrazone, acylhydrazone, urethane, acetal, or ketal group, show high antitumor activity and are water soluble and stable under physiol. conditions, and are therefore suitable for cancer treatment. Thus, transferrin was thiolated with iminothiolane; the number of SH groups introduced depended on the temperature and concentration ratio of iminothiolane to protein. Thiolated transferrin was conjugated with the 3'-amide of doxorubicin with p-maleimidophenylacetyl chloride. The product had cytostatic activity comparable to that of unconjugated doxorubicin against colon carcinoma HCT-116 cells in vitro.

IT 188985-11-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(antineoplastic transferrin and albumin conjugates of cytostatic compds. selected from anthracyclines, alkylating agents, antimetabolites, and cisplatin analogs)
RN 188985-11-7 CAPLUS
CN Hydrazinecarboxylic acid, 2-[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:89761 CAPLUS
DOCUMENT NUMBER: 128:145242
TITLE: Transferrin Conjugates of Doxorubicin: Synthesis, Characterization, Cellular Uptake, and in Vitro Efficacy
AUTHOR(S): Kratz, Felix; Beyer, Ulrich; Roth, Thomas; Tarasova, Nadya; Collery, Philippe; Lechenault, Francoise; Cazabat, Annie; Schumacher, Peter; Unger, Clemens; Falken, Ulrich
CORPORATE SOURCE: Department of Medical Oncology, Clinical Research Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Journal of Pharmaceutical Sciences (1998), 87(3), 338-346
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB One strategy for improving the antitumor selectivity and toxicity profile of antitumor agents is to design drug carrier systems employing suitable carrier proteins. Thus, thiolated human serum transferrin was conjugated with four maleimide derivs. of doxorubicin that differed in the stability of the chemical link between drug and spacer. Of the maleimide derivs., 3-maleimidobenzoic or 4-maleimidophenylacetic acid was bound to the 3'-amino position of doxorubicin through a benzoyl or phenylacetyl amide bond, and 3-maleimidobenzoic acid hydrazide or 4-maleimidophenylacetic acid hydrazide was bound to the 13-keto position through a benzoyl hydrazone or phenylacetyl hydrazone bond. The acid-sensitive transferrin conjugates prepared with the carboxylic hydrazone doxorubicin derivs. exhibited an inhibitory efficacy in the MDA-MB-468 breast cancer cell line and U937 leukemia cell line comparable to that of the free drug (employing

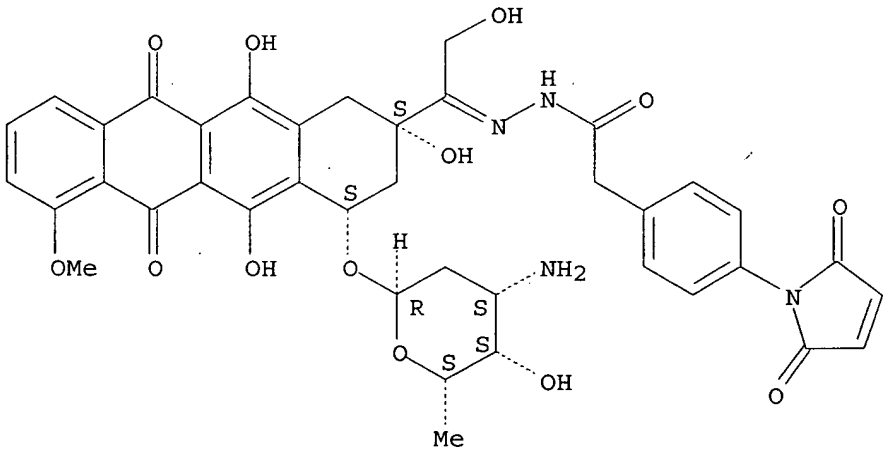
the BrdU (5-bromo-2'-deoxyuridine) incorporation assay and tritiated thymidine incorporation assay, resp., IC50 » 0.1-1 mM), whereas conjugates with the amide derivs. showed no activity. Furthermore, antiproliferative activity of the most active transferrin conjugate (i.e. the conjugate containing a benzoyl hydrazone link) was demonstrated in the LXFL 529 lung carcinoma cell line employing a sulforhodamine B assay. In contrast to in vitro studies in tumor cells, cell culture expts. performed with human endothelial cells (HUVEC) showed that the acid-sensitive transferrin conjugates of doxorubicin were significantly less active than free doxorubicin (IC50 values approx. 10-40 higher by the BrdU incorporation assay), indicating the selectivity of the doxorubicin-transferrin conjugates for tumor cells. Fluorescence microscopy studies in the MDA-MB-468 breast cancer cell showed that free doxorubicin accumulates in the cell nucleus, whereas doxorubicin of the transferrin conjugates is found localized primarily in the cytoplasm. The differences in the intracellular distribution between transferrin-doxorubicin conjugates and doxorubicin were confirmed by laser scanning confocal microscopy in LXFL 529 cells after a 24 h incubation that revealed an uptake and mode of action other than intercalation with DNA. The relationship between stability, cellular uptake, and cytotoxicity of the conjugates is discussed.

IT 202407-74-7DP, conjugates with transferrins
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation, characterization, cellular uptake, and in vitro efficacy of transferrin conjugates of doxorubicin)

RN 202407-74-7 CAPLUS

CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L4 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:75568 CAPLUS
DOCUMENT NUMBER: 128:212806

TITLE: Preparation, characterization and in vitro efficacy of albumin conjugates of doxorubicin

AUTHOR(S): Kratz, Felix; Beyer, Ulrich; Collery, Philippe; Lechenault, Francoise; Cazabat, Annie; Schumacher, Peter; Falken, Ulrich; Unger, Clemens

CORPORATE SOURCE: Department of Medical Oncology, Tumor Biology Center, Clinical Research, Freiburg, 79106, Germany

SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(1), 56-61
CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

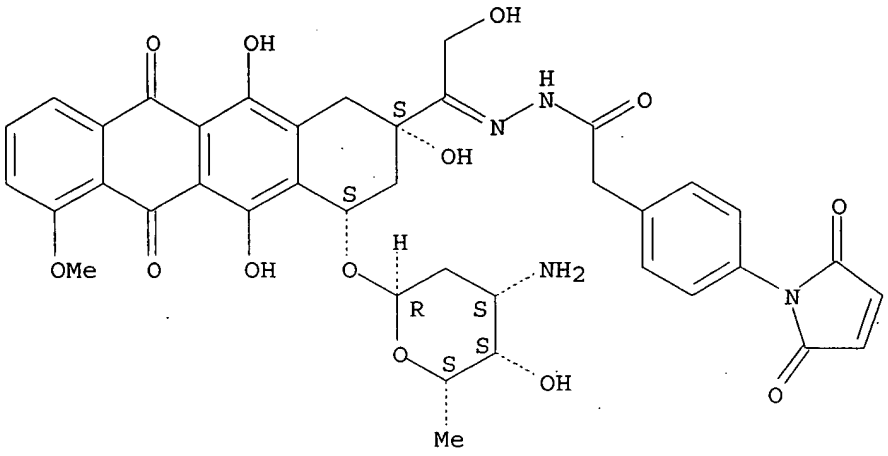
AB One strategy for improving the antitumor selectivity and toxicity profile of antitumor agents is to design drug carrier systems with suitable transport proteins. Thus, four maleimide derivs. of doxorubicin were bound to thiolated human serum albumin which differed in the stability of the chemical link between drug and spacer. In the maleimide derivs., 3-maleimidobenzoic or 4-maleimidophenylacetic acid was bound to the 3'-amino position of doxorubicin through a benzoyl or phenylacetyl amide bond and 3-maleimidobenzoic acid hydrazide or 4-maleimidophenylacetic acid hydrazide was bound to the 13-keto position through a benzoyl hydrazone or phenylacetyl hydrazone bond. The acid-sensitive albumin conjugates prepared with the carboxylic hydrazone doxorubicin derivs. exhibited an inhibitory efficacy in the MDA-MB-468 breast cancer cell line and U937 leukemia cell line comparable with that of the free drug (using the BrdU-(5-bromo-2'-deoxyuridine)-incorporation assay and tritiated thymidine incorporation assay resp., IC50.apprx.0.1-1 μM) whereas conjugates with the amide derivs. showed no or only marginal activity. These results demonstrate that antiproliferative activity depends on the nature of the chemical bond between doxorubicin and carrier protein. Acid-sensitive albumin conjugates are suitable candidates for further in vitro and in vivo assessment.

IT 202407-74-7DP, thiolated serum albumin conjugates
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and characterization and in vitro efficacy of albumin conjugates of doxorubicin against human cancer cells in relation to stability)

RN 202407-74-7 CAPLUS

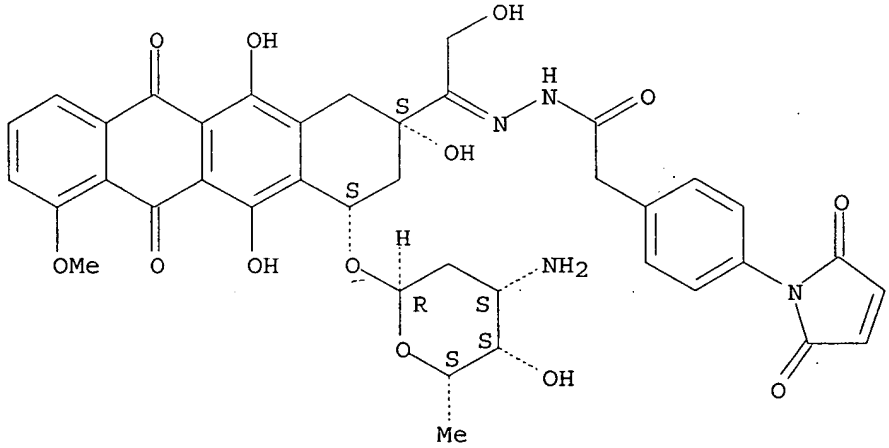
CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT 202407-74-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation and characterization and in vitro efficacy of albumin conjugates of doxorubicin against human cancer cells in relation to stability)
RN 202407-74-7 CAPLUS
CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:421308 CAPLUS
DOCUMENT NUMBER: 127:34521
TITLE: Preparation of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors
INVENTOR(S): Carr, Thomas Joseph; Desjarlais, Renee Louise;

Gallagher, Timothy Francis; Halbert, Stacie Marie; Oh, Hye-Ja; Thompson, Scott Kevin; Veber, Daniel Frank; Yamashita, Dennis Shinji; et al.

PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 253 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9716433	A1	19970509	WO 1996-US18000	19961030
W: AL, AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AZ, BY, KZ, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9609078	A	19980429	ZA 1996-9078	19961029
CA 2236111	AA	19970509	CA 1996-2236111	19961030
AU 9711180	A1	19970522	AU 1997-11180	19961030
CN 1207095	A	19990203	CN 1996-199284	19961030
BR 9612344	A	19990713	BR 1996-12344	19961030
EP 934291	A1	19990811	EP 1996-941981	19961030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
JP 2000500742	T2	20000125	JP 1997-517638	19961030
NO 9801938	A	19980629	NO 1998-1938	19980429
US 5998470	A	19991207	US 1999-290958	19990413
US 6057362	A	20000502	US 1999-330287	19990611
US 6232342	B1	20010515	US 1999-330451	19990611
US 6284777	B1	20010904	US 2000-552616	20000419
US 6331542	B1	20011218	US 2000-551968	20000419
NO 2000006716	A	19980629	NO 2000-6716	20001229
NO 2000006717	A	19980629	NO 2000-6717	20001229
NO 2000006718	A	19980629	NO 2000-6718	20001229
CN 1341590	A	20020327	CN 2001-104787	20010220
CN 1341592	A	20020327	CN 2001-104788	20010220
CN 1341593	A	20020327	CN 2001-104789	20010220
US 2002077455	A1	20020620	US 2001-839410	20010420
US 6586466	B2	20030701		
US 2002173469	A1	20021121	US 2002-160314	20020530
US 6562842	B2	20030513		

PRIORITY APPLN. INFO.:

US 1995-8108P	P	19951030
US 1995-7473P	P	19951122
US 1995-8992P	P	19951221
US 1996-13747P	P	19960320
US 1996-13748P	P	19960320
US 1996-13764P	P	19960320
US 1996-17455P	P	19960517
US 1996-17892P	P	19960517
US 1996-22047P	P	19960722
US 1996-23494P	P	19960807
WO 1996-US18000	W	19961030
US 1998-793915	A3	19980430
US 1999-330284	B1	19990611
US 1999-330305	B1	19990611

US 2000-633700 B1 20000807

OTHER SOURCE(S): MARPAT 127:34521

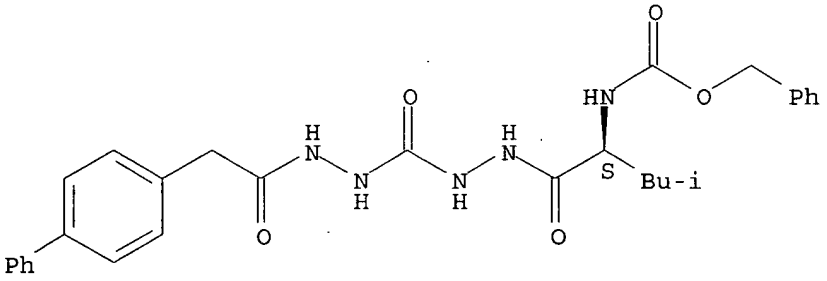
AB Title compds. of formula D-CO-Q [D = CbzNHCH(Bu-i), Cbz-Leu-NHCH(Bu-i), 4-PhOC6H4SO2NHCH2, Cbz-Leu-NHNH, etc.; Q = NHCH(Bu-i)(2-carboxythiazol-4-yl), NHCH(Bu-i)(4-carboethoxythiazol-2-yl), NHNHCOCH(Bu-i)NHCbz, CH2NHSO2C6H4-4-OPh, etc.; Cbz = PhCH2O2C] and pharmaceutical compns. of such compds., which inhibit proteases, including cathepsin K (no data) were prepared Such compds. are particularly useful for treating diseases of excessive bone loss or cartilage or matrix degradation, e.g. osteoporosis, periodontitis, and arthritis. For example, Cbz-Leu-Leu-CH2Br was treated with H2NCSCO2Et in refluxing ethanol for 4 h to give Cbz-Leu-NHCH(Bu-i)(2-carboethoxythiazol-4-yl), which was saponified by treatment with sodium hydroxide in THF to yield title compound Cbz-Leu-NHCH(Bu-i)(2-carboxythiazol-4-yl).

IT 190657-94-4P 190657-96-6P 190657-99-9P
190658-00-5P 190658-01-6P 190658-05-0P
190658-06-1P 190658-07-2P 190658-13-0P
190658-18-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydrazidyl, bis-hydrazidyl, and bis-aminomethyl carbonyl protease inhibitors)

RN 190657-94-4 CAPLUS

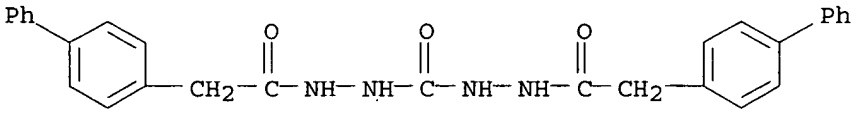
CN [1,1'-Biphenyl]-4-acetic acid, 2-[[2-[(2S)-4-methyl-1-oxo-2-[[(phenylmethoxy)carbonyl]amino]pentyl]hydrazino]carbonyl]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



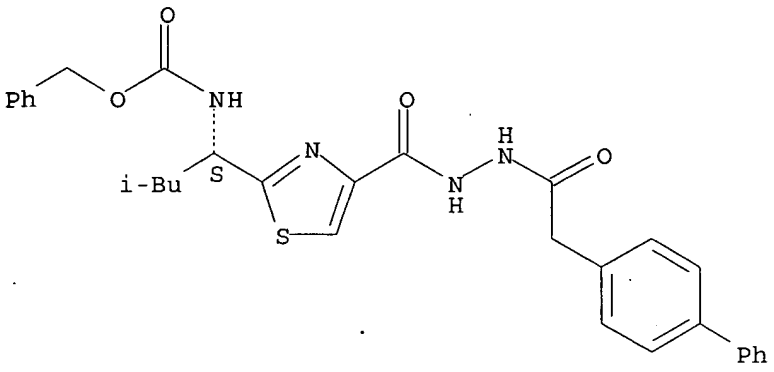
RN 190657-96-6 CAPLUS

CN [1,1'-Biphenyl]-4-acetic acid, 2,2'-carbonyldihydrazide (9CI) (CA INDEX NAME)



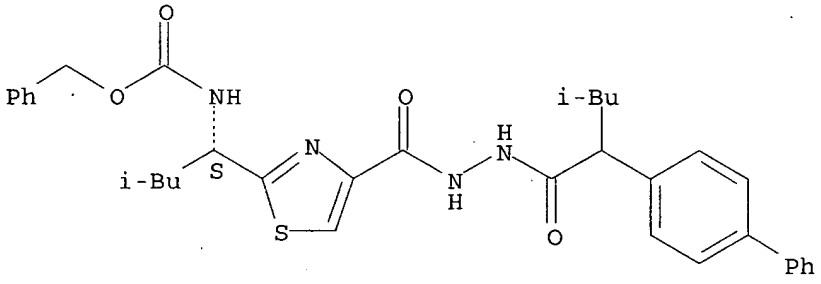
RN 190657-99-9 CAPLUS

CN [1,1'-Biphenyl]-4-acetic acid, α-(2-methylpropyl)-, 2,2'-carbonyldihydrazide (9CI) (CA INDEX NAME)



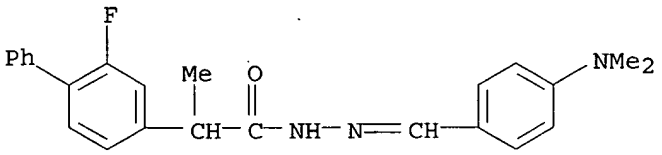
RN 190658-18-5 CAPLUS
CN 4-Thiazolecarboxylic acid, 2-[(1S)-3-methyl-1-[[(phenylmethoxy)carbonyl]amino]butyl]-, 2-(2-[1,1'-biphenyl]-4-yl-4-methyl-1-oxopentyl)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

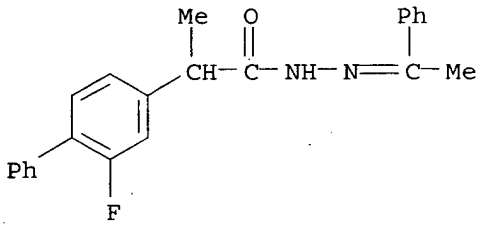


L4 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:322945 CAPLUS
DOCUMENT NUMBER: 127:265
TITLE: Synthesis and biological activity of certain flurbiprofen derivatives
AUTHOR(S): El-Sadek, Mohamed; Abdel-Aziz, Lubna; Abdel-Rahem, Kamel
CORPORATE SOURCE: Department of Medicinal Chemistry Faculty of Pharmacy, University of Zagazig, Egypt
SOURCE: Zagazig Journal of Pharmaceutical Sciences (1996), 5(1), 29-35
CODEN: ZJPSEV; ISSN: 1110-5089
PUBLISHER: University of Zagazig, Faculty of Pharmacy
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of several flurbiprofen amides and hydrazones is described. Five representative compds. were tested for pharmacol. activity; three of them exhibited superior analgesic, antipyretic and anti-inflammatory activities compared to flurbiprofen.
IT 190125-03-2P 190125-11-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of flurbiprofen derivs.)

RN 190125-03-2 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, [[4-(dimethylamino)phenyl]methylene]hydrazide (9CI). (CA INDEX NAME)

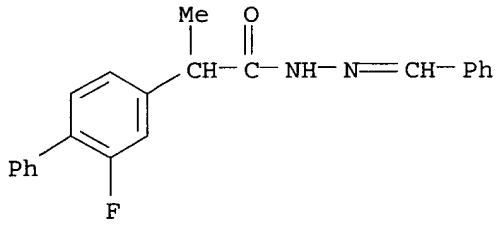


RN 190125-11-2 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, (1-phenylethylidene)hydrazide (9CI) (CA INDEX NAME)

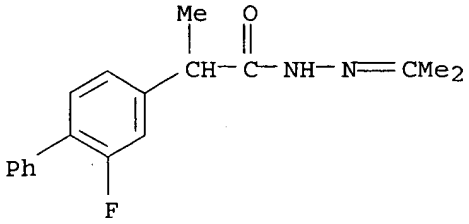


IT 190124-79-9P 190124-85-7P 190124-87-9P
190124-92-6P 190124-98-2P 190125-19-0P
190125-26-9P 190125-34-9P 190125-41-8P
190125-47-4P 190125-51-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and biol. activity of flurbiprofen derivs.)

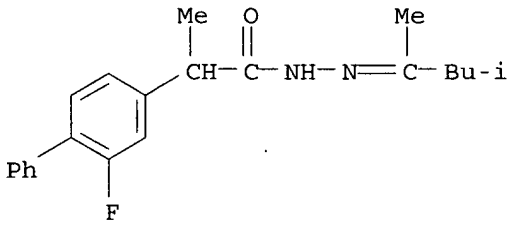
RN 190124-79-9 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, (phenylmethylene)hydrazide (9CI) (CA INDEX NAME)



RN 190124-85-7 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, (3-phenyl-2-propenylidene)hydrazide (9CI) (CA INDEX NAME)

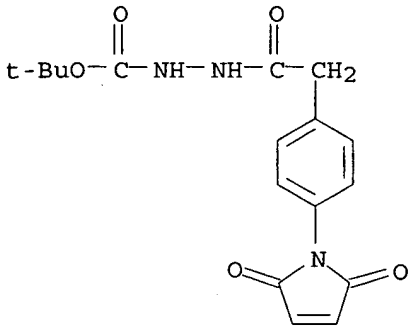


RN 190125-51-0 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-fluoro-α-methyl-, (1,3-dimethylbutylidene)hydrazide (9CI) (CA INDEX NAME)



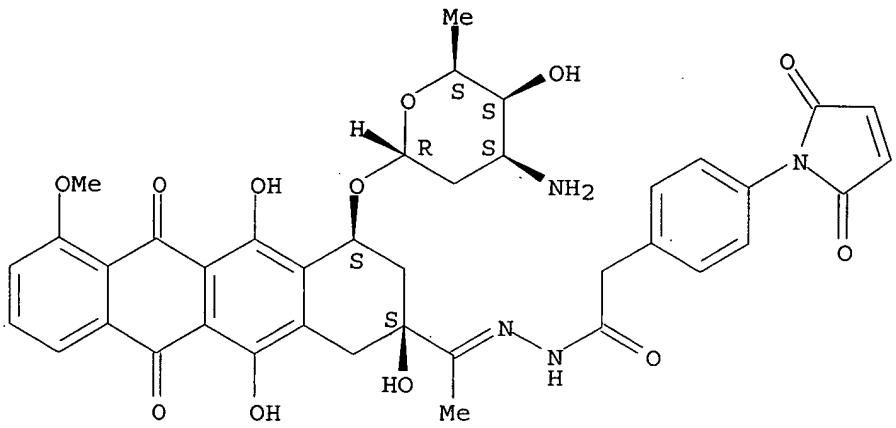
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:266884 CAPLUS
DOCUMENT NUMBER: 126:277361
TITLE: Synthesis of new bifunctional maleimide compounds for the preparation of chemoimmunoconjugates
AUTHOR(S): Beyer, U.; Kruger, M.; Schumacher, P.; Unger, C.; Kratz, F.
CORPORATE SOURCE: Abteilung Klinische Forschung, Klinik Tumorbiologie, Freiburg, D-79106, Germany
SOURCE: Monatshefte fuer Chemie (1997), 128(1), 91-102
CODEN: MOCMB7; ISSN: 0026-9247
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Bifunctional maleimide compds. are suitable for binding small mols. to carrier proteins in that they bind to the sulfhydryl group of proteins through the double bond of the maleimide group and to mols. of low mol. weight (e.g. anticancer drugs) through a functional group. Various functionalized maleimides were synthesized and characterized by 1H and 13C NMR, elemental anal., and mass spectrometry.
IT 188985-11-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bifunctional maleimides for immunoconjugates)
RN 188985-11-7 CAPLUS
CN Hydrazinecarboxylic acid, 2-[[4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]acetyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:188944 CAPLUS
DOCUMENT NUMBER: 126:277688
TITLE: Synthesis of new maleimide derivatives of daunorubicin and biological activity of acid labile transferrin conjugates
AUTHOR(S): Kratz, Felix; Beyer, Ulrich; Schumacher, Peter; Krueger, Michael; Zahn, Heike; Roth, Thomas; Fiebig, Heinz H.; Unger, Clemens
CORPORATE SOURCE: Dept. Med. Oncology, Clin. Res., Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(5), 617-622
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Maleimide groups were bound to the 3'-amino position of daunorubicin through a benzamide bond or to the 13-keto position through a benzoyl hydrazone or phenylacetyl hydrazone bond. The acid labile transferrin conjugates prepared with the latter two derivs. exhibited high activity in human melanoma cells (MEXF 989) using a clonogenic cell assay comparable to or exceeding that of daunorubicin.
IT 188944-34-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antitumor activity of maleimide-containing daunorubicins)
RN 188944-34-5 CAPLUS
CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-lyxo-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]ethylidene]hydrazide, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



● HCl

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

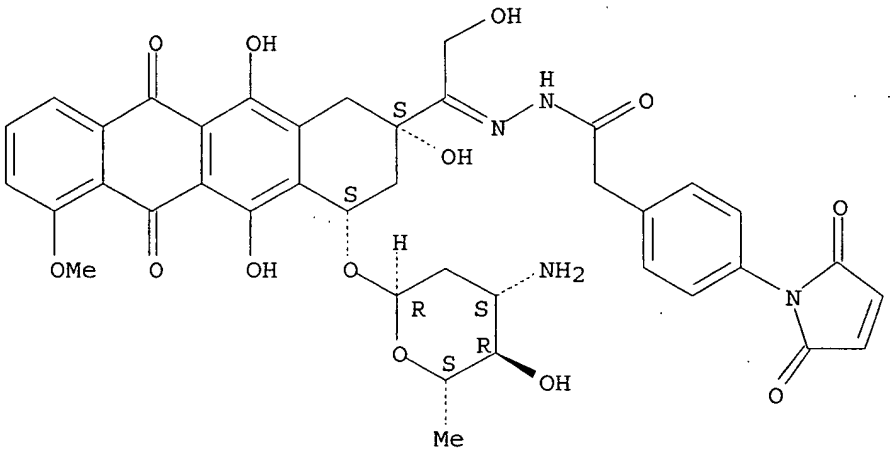
L4 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:141729 CAPLUS
DOCUMENT NUMBER: 126:242729
TITLE: Synthesis and stability of four maleimide derivatives of the anticancer drug doxorubicin for the preparation of chemoimmunoconjugates
AUTHOR(S): Krueger, Michael; Beyer, Ulrich; Schumacher, Peter; Unger, Clemens; Zahn, Heike; Kratz, Felix
CORPORATE SOURCE: Dept. Med. Oncology, Tumor Biology Center, Freiburg, 79106, Germany
SOURCE: Chemical & Pharmaceutical Bulletin (1997), 45(2), 399-401
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By attaching maleimide groups to anticancer drugs, derivs. are obtained which bind selectivity to thiolated carrier proteins. Four maleimide derivs. of the anticancer drug doxorubicin were prepared in which 3-maleimidobenzoic acid or 4-maleimidophenylacetic acid was bound to the 3'-amino position of doxorubicin through a benzoyl or phenylacetyl amide bond (1 or 2) or in which 3-maleimidobenzoic acid hydrazide or 4-maleimidophenylacetic acid hydrazide was bound to the 13-keto position through a benzoyl or phenylacetyl hydrazone bond (3 or 4). The maleimide derivs. of doxorubicin were characterized by means of 13C-NMR spectroscopy, elemental anal. and mass spectrometry. In addition, the stability of the maleimide derivs. 1-4 at pH values of 5.0 and 7.4 was investigated with the aid of HPLC. The amide or hydrazone bond of 1-4 is stable at pH 7.4 whereas the hydrazone bond is acid-sensitive.

IT 188530-68-9P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and stability of maleimide derivs. of doxorubicin for preparation of chemoimmunoconjugates)

RN 188530-68-9 CAPLUS
CN Benzeneacetic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, [1-[(2S,4S)-4-[(3-amino-2,3,6-trideoxy-α-L-arabino-hexopyranosyl)oxy]-1,2,3,4,6,11-hexahydro-2,5,12-trihydroxy-7-methoxy-6,11-dioxo-2-naphthacenyl]-2-hydroxyethylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

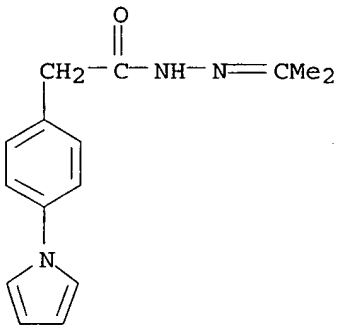
L4 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:71672 CAPLUS
DOCUMENT NUMBER: 110:71672
TITLE: Spectroscopic studies of the reaction between bovine serum amine oxidase (copper-containing) and some hydrazides and hydrazines
AUTHOR(S): Morpurgo, Laura; Befani, Olivia; Sabatini, Stefania; Mondovi, Bruno; Artico, Marino; Corelli, Federico; Massa, Silvio; Stefancich, Giorgio; Avigliano, Luciana
CORPORATE SOURCE: Dip. Sci. Biochim., Univ. Roma "La Sapienza", Rome, 00185, Italy
SOURCE: Biochemical Journal (1988), 256(2), 565-70
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyrroloquinoline quinone, the carbonyl cofactor of bovine serum amine oxidase (EC 1.4.3.6) reacts stoichiometrically and irreversibly with hydrazides of phenylacetic acid and of benzoic acid. With the phenylacetic hydrazides, a reversible intermediate step was detected by competition with substrate, carbonylic reagents, or phenylhydrazine, a typical inhibitor of the enzyme. All hydrazides formed an intense broad band with maximum absorbance in a narrow wavelength range (350-360 nm), irresp. of the acyl group, suggesting that the transition is located on the organic cofactor. A different situation was found with some phenylhydrazines, where extended conjugation can occur between the cofactor and the Ph π-electron system via the azo group, as shown by the lower energy and higher intensity of the transition. In this case, the transition was sensitive to substituents in the Ph ring. The CD spectrum of the adducts was influenced by the type of hydrazide (derived

from phenylacetic acid or benzoic acid), by pH, and by N,N-diethyldithiocarbamate binding to Cu, probably as a result of shifts of equilibrium between hydrazone-azo tautomers.

IT 112575-82-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with copper-containing amine oxidase of blood serum, spectroscopic studies of)

RN 112575-82-3 CAPLUS

CN Benzeneacetic acid, 4-(1H-pyrrol-1-yl)-, (1-methylethylidene)hydrazide (9CI) (CA INDEX NAME)



L4 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:510200 CAPLUS

DOCUMENT NUMBER: 109:110200

TITLE: Synthesis and spectral studies on some 2-N-substituted phthalimides and phthaloyl p-aminophenyloxazolin-5-ones as possible antimicrobials

AUTHOR(S): Bedair, A. H.; Lamphon, R. Q.; Ghazal, S. S.

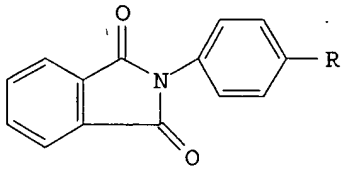
CORPORATE SOURCE: Fac. Educ., King-Abdul-Aziz Univ., Madinah Munawwarah, Saudi Arabia

SOURCE: Journal of the Serbian Chemical Society (1987), 52(8), 477-86
CODEN: JSCSEN; ISSN: 0352-5139

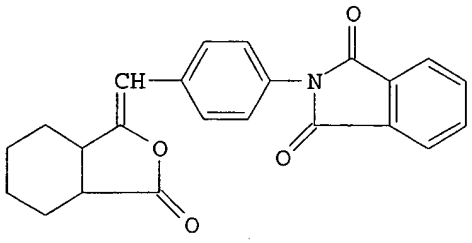
DOCUMENT TYPE: Journal

LANGUAGE: English

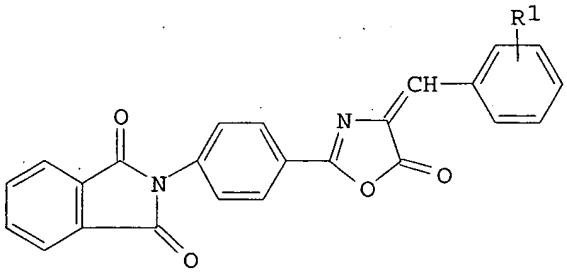
GI



I



IV



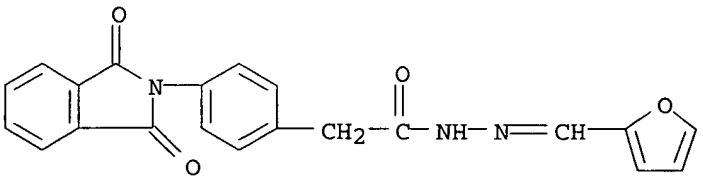
V

AB Condensation of phthalic anhydride with p-aminophenylacetic acid, p-aminohippuric acid and p-aminoacetophenone gave substituted phthalimides I (R = CH2CO2H, CONHCH2CO2H, COMe). Methylation of I (R = CH2CO2H; II) with CH2N2 gave I (R = CH2CO2Me), which reacted with N2H4 to give I (R = CH2CONHNH2; III). Condensation of II with phthalic anhydride under the Perkin reaction conditions gave benzylidene derivative IV. Reaction of III with anisaldehyde gave I (R = CH2CONH:CHC6H4OMe-4). The cyclocondensation of I (R = CONHCH2CO2H) with aromatic aldehydes in Ac2O in the presence of fused AcONa gave oxazolinones V (R1 = 3-, 4-OH, 4-OMe, 4-NMe2). I (R = CH2CO2H, COMe, CH2CONHNH2, CH2CO2Me, CH2CONHN:CHC6H4OMe-4) and IV were tested for antibacterial activity, and showed moderate activity. I (R = CH2CONHNH2) was the most active.

IT 115978-05-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation reaction with phenylphthalimide derivative)

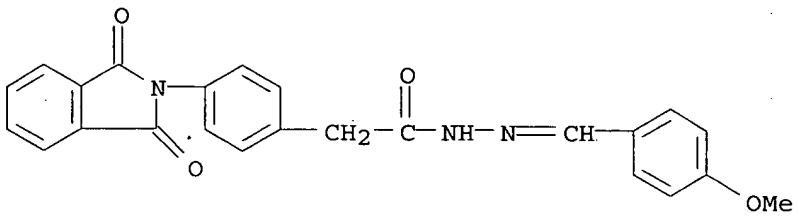
RN 115978-05-7 CAPLUS

CN Benzeneacetic acid, 4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, (2-furanylmethylene)hydrazide (9CI) (CA INDEX NAME)

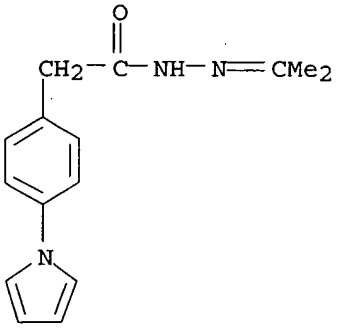


IT 115978-04-6P

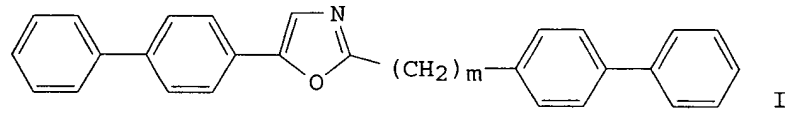
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 115978-04-6 CAPLUS
CN Benzeneacetic acid, 4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, [(4-methoxyphenyl)methylene]hydrazide (9CI) (CA INDEX NAME)



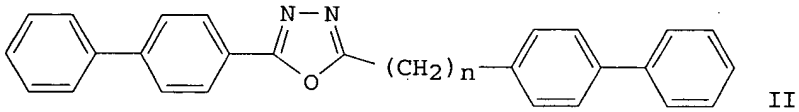
L4 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:218096 CAPLUS
DOCUMENT NUMBER: 108:218096
TITLE: Inhibition of copper-dependent amine oxidases by some hydrazides of pyrrol-1-ylbenzoic and pyrrol-1-ylphenylacetic acids
AUTHOR(S): Artico, Marino; Corelli, Federico; Massa, Silvio; Stefancich, Giorgio; Avigliano, Luciana; Befani, Olivia; Marcozzi, Giordana; Sabatini, Stefania; Mondovi, Bruno
CORPORATE SOURCE: Ist. Chim. Farm. Tossicol., Univ. Roma "La Sapienza", Rome, Italy
SOURCE: Journal of Medicinal Chemistry (1988), 31(4), 802-6
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:218096
AB Some hydrazides of pyrrol-1-ylbenzoic and pyrrol-1-ylphenylacetic acids were prepared and their effect on copper-dependent amine oxidases (Cu-AOs) and FAD monoamine oxidases (MAOs) activities was tested. The compds. were not substrates for Cu-AO, but acted as noncompetitive inhibitors. Hydrazides of pyrrol-1-ylphenylacetic acids were highly specific for plasma amine oxidase (Ki = 0.5-1 μM). In contrast, all the hydrazides were weak inhibitors of MAO activity. Incubation with the hydrazide derivs. led to irreversible inactivation of Cu-AOs. Therefore, the inhibition implied 2 distinct steps. The 1st one consisted of the rapid formation of the enzyme-inhibitor complex and was reversed by dialysis. In the 2nd step, the complex was irreversibly transformed, probably by the formation of a Schiff base between the hydrazide and the prosthetic carbonyl group of the enzyme.
IT 112575-82-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and copper-dependent amine oxidases inhibition kinetics with)
RN 112575-82-3 CAPLUS
CN Benzeneacetic acid, 4-(1H-pyrrol-1-yl)-, (1-methylethylidene)hydrazide (9CI) (CA INDEX NAME)



L4 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:636613 CAPLUS
DOCUMENT NUMBER: 107:236613
TITLE: 2-(O-Biphenylylpolymethylene)-5-biphenylyl-1,3-oxazole and 2-(ω-biphenylylpolymethylene)-5-biphenylyl-1,3,5-oxadiazole
AUTHOR(S): Zhou, Yimin; Xiao, Changhe; Wang, Shenxiu
CORPORATE SOURCE: Dep. Chem., Nankai Univ., Tianjin, Peop. Rep. China
SOURCE: Gaodeng Xuexiao Huaxue Xuebao (1987), 8(1), 52-4
CODEN: KTHPDM; ISSN: 0251-0790
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
GI

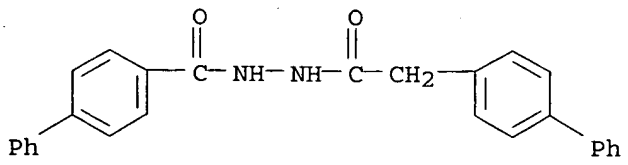


I



II

AB Title compds. I (m = 1, 2, 3) and II (n = 1, 2, 3, 4) were prepared and their IR, UV, NMR, mass, and fluorescence spectra were reported.
IT 111678-07-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)
RN 111678-07-0 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, 2-([1,1'-biphenyl]-4-ylcarbonyl)hydrazide (9CI) (CA INDEX NAME)



Saloni Sharma 07/18/2006